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*Meyer, E., and Arnold, L., Amer. J. Digest. Dis., 5:418.

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DOUBLE URETER IN THE CHILD

By F. Douglas Stephens

Royal Children's Hospital, Melbourne

THE purpose of this paper is to record the significant findings of a five-year study of double ureter in the child, a condition which has presented many problems in diagnosis and management at the Royal Children's Hospital, Melbourne.

This study was undertaken by the urological clinic of this hospital. We have been able to assemble the material set out below. Most of the patients were new, four only having been under observation for long periods.

There were 28 infants and children, 24 female and 4 male, in whom the ureter was duplicated; in 6 of these the double ureter was bilateral and in every instance of bilateral reduplication the patient was a female. Twenty-two of the double ureters occurred on the right side and 12 on the left (Table 1).

This difficult subject has called for investigation because of the lack of adequate explanation of many of its symptoms and signs; because of the recurrence of infection following standard methods of treatment; and because of inadequate knowledge of the morbid physiology of this condition and of its contingent anomalies.

We have been able to extend our knowledge in these respects by the routine, assiduous and comprehensive use of the method of micturition cysto-urethrography, a method of urography practised extensively in children by Brodny and Robins (1948); by the use of radiography during the act of voidance of radio-opaque urine, it was possible to demonstrate not only the key anatomical anomalies, but also their debilitated functions, otherwise unappreciable.

Double ureter disease is highly complex, but as we have accumulated knowledge the reasons for the inscrutability of double ureter disease have become more apparent. It must now be acknowledged that the obvious double ureter anomalies do not explain the whole clinical story. There is often a complete, but less obvious derangement of the physiology of the whole urinary system, of which we have not hitherto taken full account.

For instance, it has been shown that normal healthy girls rarely, if ever, exhibit vesico-ureteral reflux (Stephens, 1955), but that girls who have double ureter on one side frequently show ureteral reflux in one or both components of this double ureter, and even in the opposite healthy looking ureter (Fig. II) because of the widespread disturbances of the physiology of the urinary tract.

We have been able by the use of micturition cysto-urethrographic methods of investigation, in conjunction with intravenous pyelography and retrograde pyelography, to establish satisfactorily which of the ureters is physiologically or anatomically unsound; to offer, in most cases, a reasonable explanation for infection in cases of double ureter; and to incriminate other unsuspected anomalies in cases of double ureter, the infections from which have not been cured by routine methods.

We have been able to show clearly the presence of megaureters, of ureterocoele, of ureteral reflux — all precursors of infection —

and often to establish their presence on the unsuspected other side.

As a result of the diagnostic methods mentioned above, disturbances of renal function, such as renal hypoplasia or obstructive hydronephrosis, have become apparent.

Factors such as these may determine the whole principle of treatment. It has not been uncommon to find that there is disease of the opposite ureter, hitherto undiscovered, which demands a totally different management appropriate to the obviously affected side.

paper (Stephens, 1954). But a brief description will be repeated here together with those variations pertinent to the double ureter problem. Also included will be the details of the double micturition test — a simple but important clinical test — and of triple micturition therapy.

The technique is simple: With the child or baby lying prone on the X-ray table sufficient 16 per cent. Diaginol is introduced into the bladder to fill it to capacity. X-ray films of the bladder and upper and lower urinary tract are then taken when the bladder is full

TABLE 1

ANALYSIS OF CASES

Total number of cases	28
Bilateral cases	6
Total number of double ureters	34
Sex incidence	24 Females 4 Males — F. 85.7 per cent.
Side affected (34 double ureters)	22 Right 12 Left — R. 64.7 per cent.
Number of double ureters in each group:	
External Ectopic	Group I — 1
Urethral Ectopic	Group II — 12
Vesical Ectopic	Group III — 13
Conjoined Double Ureter	Group IV — 7
	Unclassified — 1

TECHNIQUE OF MICTURITION CYSTO-URETHROGRAPHY

This radiographic procedure displays the bladder, the urethra, and sometimes the ureters by reflux, either during the resting phases when the bladder is acting as a reservoir, or during the act of micturition when intravesical pressures, more than treble that of the ordinary resting bladder pressures, are brought to bear on the ureteral orifice.

This technique offers the most reliable test of competence of the uretero-vesical valve mechanism, a mechanism which in normal children is competent to resist reflux, but which in double ureter patients and in idiopathic megaureters, is incompetent.

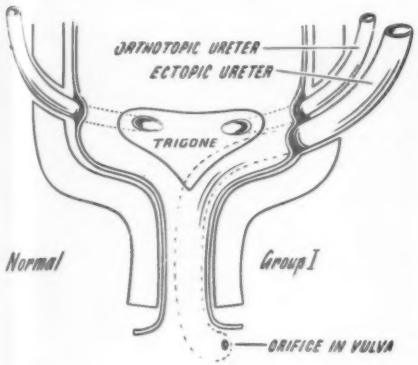
Our technique of micturition cysto-urethrography has been described in a previous

and during micturition. An immediate post-micturition film will demonstrate the presence and site of any residual content in the urinary tract.

The double micturition test is "positive" when, after a normal act of micturition, the child can pass more urine two minutes later. The suspected explanation of this phenomenon is ureteral reflux but radiographic confirmation is necessary.

A further act of micturition two minutes later — triple micturition — has been found, in cases of idiopathic megaureter, to empty out all the residual urine caused by that ureter (Stephens, 1954). These observations resulted from micturition cysto-urethrographic studies and triple micturition is now applied daily as a therapeutic means of eliminating the residual urine. Previously, we have

recommended triple micturition more frequently in the day (Stephens, 1954) but we now find that once daily is sufficient as a prophylactic measure.



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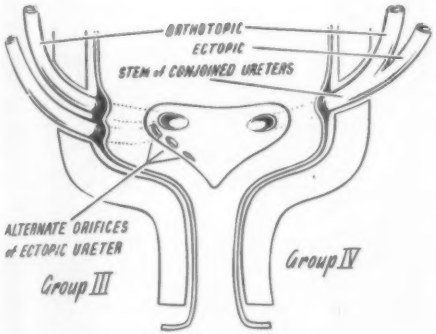

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FIG. I. Diagram demonstrating the course of the double ureters in (A) Group 1 (external ectopia), (B) Group 2 (urethral ectopia), (C) Group 3 (vesical ectopia) and Group 4 (conjoined).

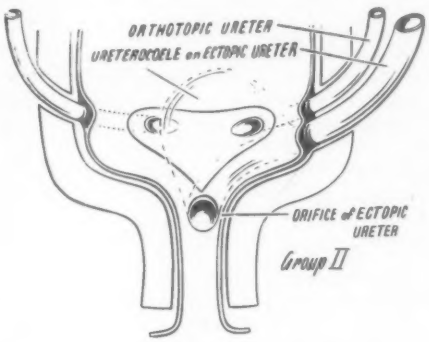
NOMENCLATURE

We have termed the ureter draining the upper portion of the double kidney the ectopic ureter; that draining the lower portion the orthotopic ureter; and the single ureter on the opposite side, the opposite or contralateral ureter. When an ectopic and orthotopic ureter join cranially to the bladder to form a single ureter with a single orifice at the normal site, we call it a conjoined ureter.

Ectopic ureter arising in a single kidney, an entirely different problem, is not discussed in this paper.

CLASSIFICATION OF DOUBLE URETER DISEASE

Some reference to the embryological hypothesis of the origin of double ureters will help to clarify their type and classification.



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Except in rare instances, double ureters, whether they are complete or incomplete in their duplication, are derived from two ureteric buds. These arise either separately from the Wolffian duct or as a single outgrowth which splits into two at any point along its course (Hawthorne, 1936; Higgins *et alii*, 1951). Thus any combination in the duplication is possible.

In this paper double ureter disease is classified into groups according to location of the ectopic ureteric orifice (Fig. I). The classification falls naturally into four categories (Table 1).

Group I, external ectopic ureter when the orifice lies outside the urinary tract.

Group II, urethral ectopic ureter, when the orifice lies in the urethra in the female, or in the male in the prostatic urethra, or the Wolffian derivatives, namely the ejaculatory ducts or vesicles.

Group III, vesical ectopic ureter, when the ectopic orifice opens independently into the bladder.

Group IV or conjoined double ureters in which the ectopic and orthotopic ureters meet to form a common stem, opening as one orifice in the orthotopic situation in the bladder.

Each group has its distinguishing feature: the external ectopic ureter causes persistent wetting; the urethral ectopic ureter, when opening low in the urethra causes wetting but if high the orifice becomes obstructed by the tonic closure of the internal sphincter, causing all the characteristic secondary effects of obstruction in that ureter, notably, ureterocoele formation and very early infection; the vesical ectopic ureter may pass unnoticed unless one or both ureters should be complicated by reflux, or idiopathic dilatation predisposing to chronic infection; conjoined ureters are subject to occasional attacks of pyelitis.

THE ECTOPIC URETER

The ectopic ureter is the conspicuous abnormal element in double ureter disease (Fig. I). It is for this reason that it is often taken for granted that it is the only source of the infection though it is, in many cases, the main cause of symptoms. The orthotopic and to some extent the opposite ureter are also affected, though often not prominently. In point of fact, the whole urinary tract usually contributes to the clinical pattern.

The cause and relation of the ectopic ureter

The ectopic ureter drains the upper portion of a double kidney. The renal parenchyma is well developed when the ureter is normal in calibre but is frequently thinned out by obstructive hydronephrosis or by hypoplasia when the ureter is large.

The ureter issues either from the upper major calyx or independently from one or two minor calyces, passes anterior to the pelvis of the lower segment, crosses the orthotopic ureter from the medial to the lateral side — here it may join the orthotopic ureter to form a common stem — then turns medially, lying lateral to the orthotopic ureter, to enter a common tunnel through the muscle of the bladder wall.

From here both ureters run a submucous course, variable in length in the case of the ectopic ureter, and in that of the orthotopic ureter, terminating in the lateral horn of the trigone.

We found that these ureters open into the bladder either by an ampulla or septate orifice — the ectopic ureter being lateral; or they part company, the ectopic orifice coming to lie on the outer lip, or on the inferior margin of the orthotopic orifice, or perhaps more distally along the lateral and inferior margin of the trigone (Fig. Ic).

FIG. II. B.V., female, aged 17 years, right double ureter. Micturition cysto-urethrogram showing vesico-ureteral reflux up all three ureters. Arrow indicates point of ligation of right ectopic ureter five years previously.

In females other longer submucous ectopic ureters open beyond the confines of the bladder into the posterior wall of the urethra (Fig. Ib) or on to the side of the external urethral orifice in the vulva (Fig. Ia).

In males, the orifice opens into the posterior urethra as far distally as the verumontanum, or, as in one case, somewhere into the genital ducts.

These ectopic urethral ureters become obstructed in the resting phases of the bladder by the grip of the contracted internal urethral sphincters. It is only during micturition phases that this sphincteric obstruction is released.

ORTHOTOPIC URETER

This term is applied to the ureter which drains the lower portion of a double kidney.

The orthotopic ureter may often conceal, in a case of double ureter, as much or more disease than the ectopic ureter itself. For instance, as many as 18 out of 24 orthotopic ureters in the urethral or vesical ectopic groups were abnormal. Free reflux occurred in eighteen. Thirteen of these were megaureters, though they showed no evidence of obstruction (Table 2).

It is not unusual for the orthotopic ureter to be dilated or diseased even when its sister ectopic ureter is normal in calibre and function (Fig. III).

TABLE 2

CLASSIFICATION OF URETERS, ECTOPIC, ORTHOTOPIC AND OPPOSITE, TO SHOW NUMBERS IN ALL GROUPS, AND THE INCIDENCE OF REFLUX IN RELATION TO CALIBRE OF THE URETERS

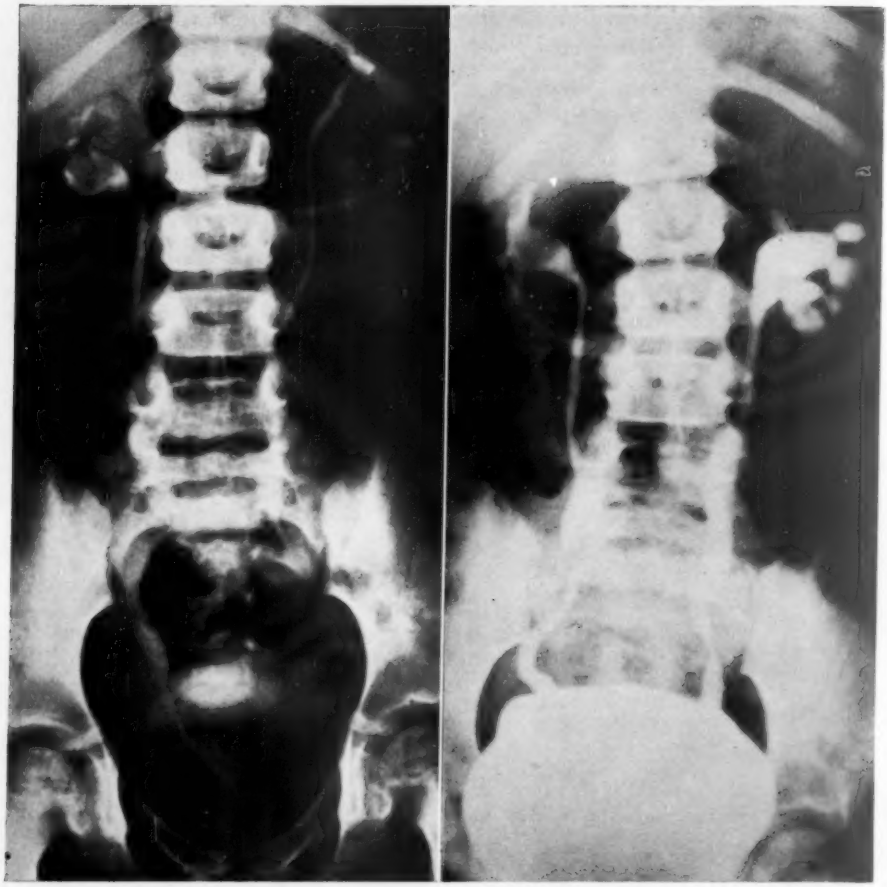
Group	*Number of Ureters in Each Group*	*Total Ureters*	*Normal Calibre*	*Megaureter*	*Reflux*
I (External Ectopic Group)	2 ureters	Ectopic 1	0	1 (idiopathic)	0
		Orthotopic 1	1	0	0
		Opposite*	–	–	–
II (Urethral Ectopic Group)	30 ureters	Ectopic 11	0	11 (obstructing)	2
		Orthotopic 11	3	0	0
				8 (idiopathic)	8
		Opposite* 8	7		1
				1 (idiopathic)	1
III (Vesical Ectopic Group)	34 ureters	Ectopic 13	10		1
		Ectopic		3 (idiopathic)	3
		Orthotopic 13	8		5
		Orthotopic		5	5
		Opposite* 8	8	0	4
IV (Conjoined Double Ureters)	12 ureters	Stem of conjoined ureters 7	7	0	0
		Opposite* 5	5	0	0
	78†				30

†All 78 ureters in this table open into the bladder or at a site more caudal. Nine ureters (3 cases) are omitted because reflux was not tested by micturition cysto-urethrography.

*In bilateral cases, where the opposite ureter is also a double ureter, it is included, in this table, in the group to which it belongs.

Apart from these, only one child showed an actual stenosis of the ectopic orifice, the ostium affected being that of the external ectopic ureter.

Ectopic ureters were found to exhibit other abnormalities in addition to their varying sites of termination. Megaureter of both obstructive and idiopathic types, ureterocoele and ureteral reflux occurred frequently. All these conditions are described more fully under separate headings.



A B

FIG. III. W.A., female, aged 6 years. Case of double left ureter showing widespread vesico-ureteral reflux.

A. I.V.P. showing normal function and calibre right kidney and ureter and left ectopic kidney and ureter but poor iodide concentration in the left orthotopic kidney.

B. Micturition cysto-urethrography demonstrates free reflux into normal calibre right ureter and pelvis, and slightly enlarged left orthotopic ureter and pelvis.

OPPOSITE URETER

In every instance in which the double ureter was unilateral, with one exception the opposite or contralateral ureter was of normal size. In the exception noted the opposite ureter was slightly enlarged in calibre: in this child, and in 5 others, ureteral reflux occurred (Table 2).

When ureteral reflux occurred up the opposite ureter, either one or both of the double ureters were similarly affected, showing again the widespread derangement of function in double ureter disease.

URETERAL REFLUX

Ureteral reflux can occur from the bladder to the ureter (vesico-ureteral reflux); from ureter to ureter (uretero-ureteral reflux); and from the urethra to ureter (urethro-ureteral reflux).

Reflux is not only a common but also a most important feature of double ureter

disease. It is important because refluxed urine is residual urine, which is a fertile cause of infection.

Ureteral reflux has no relation to megaureter. Investigations show that ureters that have been subject to free reflux from birth up to seventeen years show no suggestion of megaureter (Fig. II). Furthermore, repeated radiographic examinations of non-obstructive megaureters which show marked reflux have shown no increase in calibre of such ureters.

Therefore, megaureter is neither the cause of reflux, nor is reflux the cause of megaureter.

Vesico-ureteral reflux

One would not expect that reflux would occur much more frequently in the orthotopic than the ectopic ureters, but this is so (Table 2). This is shown in Group II (urethral ectopic) and in Group III (vesical ectopic). In these groups, reflux was found in only 6 of the 24 ectopic ureters (25 per cent.); but reflux was present in 18 of the 24 orthotopic ureters (75 per cent.).

Thus, in regard to reflux, the orthotopic ureter is a bigger factor in infection than the more pathological looking ectopic ureter.

Ureteral reflux even occurred in the single opposite ureter in 6 cases, only one of which was slightly enlarged above normal calibre: another observation which indicates the extent of the derangement of the whole urinary system in double ureter disease.

Uretero-ureteral reflux

In Group IV (conjoined ureters) 7 cases of double ureter, each of which had joined to make a common stem before opening into the bladder, were studied. Here vesico-ureteral reflux had not occurred. It was, however, possible radiographically to show, by injection of iodide solution into one pelvis of a double kidney, that reflux occurred into the other as described by Campbell (1951a) and this happened whether the ureters were enlarged or not.

It was possible clearly to demonstrate (Fig. IV) that in a particular example of megaureters joining to form a common stem of normal calibre, this reflux caused delay in emptying of at least one hour. This residual urine content was enough to bring about a serious infection.

Urethro-ureteral reflux

In our studies this was the most uncommon type of reflux. It was limited to the ectopic ureters in Group II (urethral ectopic orifice). In 11 such ectopic ureters the reflux was demonstrable in only 2 and it occurred only during micturition, since in the intervals the bladder was excluded from the urethra by the contracted urethral sphincter muscles. In one case the ureter, which contained the refluxed urine, remained distended for at least an hour after micturition (Fig. V). This urine was retained in the ureter because its orifice became obstructed by the urethral sphincter in the quiescent phases between voiding. This is a point which should be remembered in searching for sources of chronic infection in a case of double ureters.

MEGAURETER

Megaureter literally means abnormally large ureter. A feature of double ureters, the term includes both obstructive and idiopathic (non-obstructive) dilatations. Megaureter is a frequent occurrence in the complex pathological pattern associated with double ureter disease. Whether the dilatation is obstructive or idiopathic the consequent residual urine leads to urinary infection.

Obstructive megaureters were observed only in ectopic ureters; they were grossly dilated, elongated and tortuous, and were surmounted by a hydronephrotic kidney.

In contrast to them, the idiopathic, non-obstructive megaureters were more frequently orthotopic. In general, they were less enlarged and less tortuous than those of the obstructive type. And in this group, the kidney substance was better preserved, though in some cases the appearances suggested hypoplasia.

A mixture of obstructive and non-obstructive (idiopathic) megaureters, and normal calibre ureters has been frequently seen in our cases.

The chief cause of obstruction in our 13 cases of megaureters with obstruction, was the intermittent pressure of the urethral sphincters, predominantly the internal, on the orifice and terminal end of the misplaced

FIG. IV. L.W., female, aged 4½ years. Right conjoined megaureters meeting to form a common ureter of normal calibre.

A series — To show delayed emptying and ureter-to-ureter reflux on retrograde pyelo-ureterogram. These films were taken at approximately ten-minute intervals with no further injection of iodide.

B series — To show emptying of ureters by triple micturition two months after uretero-vesical meatotomy. Fig. Ib shows cystogram with slight reflux; IIb shows reflux immediately after first micturition (some iodide in vagina); IIIb shows ureteral reflux four minutes later immediately after voiding; IVb after passing small amount of urine five minutes later, and Vb after further micturition showing urinary tract clear of iodide.

urethral ectopic ureters of Groups I and II. The orifices of 10 of these ectopic ureters were abnormally wide, in fact wide enough to admit with ease the beak of a 16 French resectoscope. In one case only was the external ectopic orifice actually stenotic. In 2 others the fact that the orifices were invisible suggested a degree of stenosis. No instance of the so-called achalasia type of ureteral obstruction was seen.

In these cases the terminal end of the ureter and its orifice lay within the grasp of the urethral sphincters. It was only during micturition, when the sphincter relaxed that obstruction ceased and the ureter was able to discharge its urine. In the intervals, the ureter was firmly obstructed, with consequent stagnation and infection. Fig. V demonstrates the obstructive action of the internal sphincter on the terminal end of the ureter.

Idiopathic megaureters, in both the urethral and vesical ectopic groups, occurred in thirteen orthotopic ureters and in three ectopic ureters. Idiopathic megaureters resemble in all respects those bilateral megaureters with reflux which were described in a previous article (Stephens, 1954).

These ureters undergo active peristalsis, empty their contents rapidly, and are subject to free reflux which leads to residual urine and infection. Their ureteral orifices generally appear normal but can be patulous, even in the degree seen in one child in whom the orifice was so large that the 20 French panendoscope sheath could be passed freely up the lumen of the ureter. There was, however, no specific evidence of obstruction in these idiopathic megaureters.

We consider that idiopathic megaureter is a predetermined abnormality of the ureteric bud; that the degree of dilatation is stable in any one child; that peristalsis is active and co-ordinated; that vesico-ureteral reflux, which is not confined to megaureters, is a separate additional anomaly affecting the ureterovesical junctions of all these idiopathic megaureters; and that obstruction either of the ureter or the bladder neck is non-existent. In short, the ureter is developmentally enlarged, but lacks its uretero-vesical valve mechanism.

Ureterocoele

In children there are two types of ureterocoele. The more uncommon variety is the intravesical globular dilatation of the terminal end of a single ureter, the meatus of which is stenosed but opens at the normal site on the trigone. This type is not dealt with in this paper.

The second and common type is the globular vesical submucous enlargement of frequent occurrence in association with ectopic ureter. The ureteric orifice is larger in diameter than normal, lies in the urethra, and is gripped, except during micturition, to the point of occlusion by the sphincters of the urethra. The ureter, lying under the trigonal mucosa, distends in globular shape into the lumen of the bladder (Fig. Va) — sometimes to such a size that it almost fills this organ. But once micturition begins, the urethral sphincters relax, ureteral peristalsis occurs and the ureterocoele empties.

Cystoscopic views were obtained of the ureterocoele in its distended state, and also during its phase of active peristalsis when the ureterocoele contracted as a ureter and vanished in its trigonal course, remaining visible only at its orifice in the urethra.

We believe this type of ureterocoele is wholly due to the obstructive effects of the urethral sphincters. The ureterocoele is itself not seriously obstructive to the urethra.

In this series of 12 urethral ectopic ureters, ureterocoeles were identified by cystourethrography or cystoscopy in ten.

In 2 of these 10 ureterocoeles, we could also show that, instead of remaining empty soon after micturition began, the ureterocoele actually refilled by reflux with iodide solution which replaced the urine voided during micturition (Fig. V). In both of these children, and in only these children, prolapse of the ureterocoele occurred through the external urethral orifice during micturition. Reflux is therefore the probable explanation for the uncommon symptom of prolapse. The refilled ureterocoele provides a bolus which is expelled by bladder contraction towards the end of micturition.

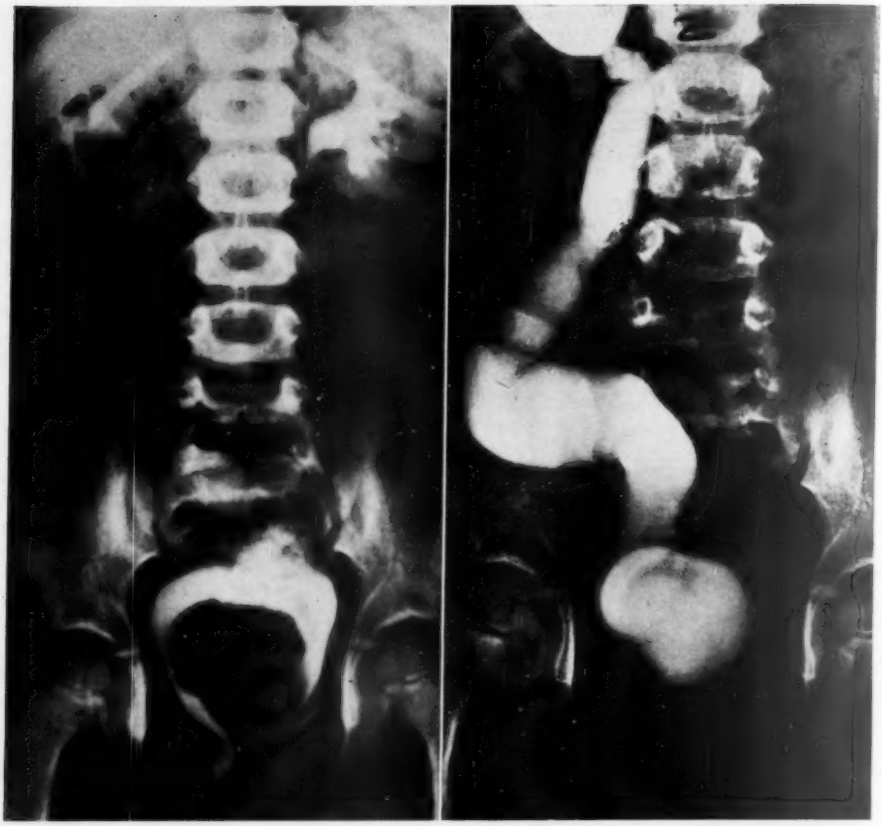


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FIG. V. E.B., aged 4 years, female, with right double ureter and ureterocoele on the urethral ectopic ureter.

A. Showing filling defect of ureterocoele in bladder in the fifty minute I.V.P. series.

B. Micturition cysto-urethrogram series showing iodide locked in the ectopic ureter and ureterocoele by the grasp of the internal sphincter. This X-ray was taken one hour after micturition had emptied the bladder but filled the ureterocoele and ureter by reflux. Note that the ureter and ureterocoele still contain much residual urine and that the obstruction to the ureter caused by the internal sphincter was complete during the filling phase of bladder function.

THE PROPER ORDER OF INVESTIGATION IN A CASE OF PYURIA IN A CHILD: A SUSPECTED CASE OF DOUBLE URETER

Adherence to a standard order of investigation will avoid repetitions, expedite an over-all diagnosis, and often save unnecessary procedures and expense. This order is as follows:—

1. Routine urine and blood tests.
2. Double micturition test: This should be applied to any case of pyura in children over eighteen months of age. A second sample of urine passed two minutes after the first indicates presence of residual urine.
3. Micturition cysto-urethrography to confirm the existence of reflux.
4. The assessment of renal function by intravenous pyelography, the technique being modified by the use of an indwelling catheter to keep the bladder empty. Misinterpretations of function arising from reflux are prevented by this modification.

5. When finding by the double micturition test is in the negative, proceed with the routine technique of intravenous pyelography. But should these measures fail to demonstrate a reason for infection, micturition cysto-urethrography becomes necessary. A ureter which looks normal on intravenous pyelogram may have a defective uretero-vesical sphincter permitting reflux which is only demonstrable by this technique.
6. Routine cystoscopy and retrograde pyelography are usually necessary to complete the examination.

TREATMENT

Having determined the anomalous anatomy and the nature and extent of the pathological conditions it has evoked, and mindful of the functional disturbance, we can more or less "blueprint" the management.

As in other diseases success lies in early diagnosis followed by early treatment, and with the modern effective diagnostic methods there is little reason why this should not be attained.

Triple micturition is not only a means of early diagnosis; it is also a method of treatment of reflux retention. If triple micturition is persisted in and constantly practised, it can permanently eliminate any urinary stasis which, if allowed to remain, could soon lead to pyuria and renal destruction. Because triple micturition has successfully removed the refluxed urine in these cases, we have not had reason to perform the operation designed by Hutch (1952) to prevent reflux.

Treatment by triple micturition may sometimes suffice for the elimination of residual urine; but double ureter cases often involve more intractable types of urinary retention. Here there is superadded ureteric obstruction from compression by the urethral sphincters which further increases the ureteral retention, favouring infection, and damaging renal parenchyma by back pressure effects.

In these circumstances the difficulties of conservative treatment are greatly increased. Nevertheless, triple micturition combined with modern chemotherapy and specific antibiotics will often sterilize the urine. When definite obstruction is present in one or more of the ureters, these measures alone are insufficient.

We meet eventually the patient who fails to respond to the best planned and most faithfully implemented medical treatment, and resort to radical surgery seems imperative. But before doing so it is proper to weigh the potentialities of conservative surgery.

Conservative surgery

This practically means an attempt to salvage the obstructed and damager ectopic ureter, and to decompress the corresponding renal segment before it deteriorates any further. The main objective is surgically to overcome the obstruction of the ectopic ureter while at the same time keeping non-surgical methods of double ureter treatment at their highest pitch.

In 3 cases the orifice of the ectopic ureter was transposed surgically from the urethra where it was intermittently obstructed by the sphincters to the bladder. Here there was no obstruction but instead vesico-ureteral reflux ensued. The ureterocoele when present was partially or totally deroofed. This procedure can be done by transurethral resection or by open operation.

In this way, the deterioration in the kidney substance from obstruction was arrested, and infection was overcome by resort to antibiotics in infants, and in older children to triple micturition which was necessary because of the reflux.

The surgery of the ectopic ureter

As the management becomes better understood, the more radical surgical measures are less frequently required. They are reserved for the patient who continually wets because of a misplaced ureteral orifice or who seeks medical aid in the later stages of the disease when the ectopic segment of kidney is reduced by obstruction or infection to a useless shell. Then unhesitant, carefully planned surgery is the treatment of election.

The surgeon will have before him a complete "blueprint" of the disease problem which he has gleaned from the diagnostic survey. He will have discovered which ureters are faulty, and which kidneys are functionally reliable.

The ectopic ureter and its diseased extensions are the chief targets of this surgery, though it is to be remembered that other parts of the urinary system are also involved.

It is often a question of pruning the diseased parts, leaving enough kidney parenchyma with satisfactory drainage for the maintenance of life and health.

We employed nephrectomy when both halves of a double kidney were functionally useless and hemi-nephrectomy when one part only was beyond salvage. These techniques are adequately described elsewhere (Campbell, 1951b; Gross, 1953a).

When reflux is present, the nephrectomy or hemi-nephrectomy should be combined with total ureterectomy. In one child, it was necessary to remove the defunct ectopic half of the kidney, its ectopic ureter not only down to the bladder, but also the submucous intravesical and urethral extensions from within the bladder. These extensions were dissected submucously through an incision along the border of the trigone. In another child the ureter was removed to the level of the bladder and the ureterocoele was simply marsupialized into the bladder and urethra.

An essential difference is apparent in the management of the ureterocoele on the reflux urethral ureter from that on the non-reflux ureter. In the former type, in our two cases, the ureterocoele had prolapsed through the urethra during micturition. It was therefore necessary in this type to remove the ureterocoele or marsupialize its roof to obviate recurrence of prolapse. In the latter and more common type which does not prolapse, the ureterocoele was neglected entirely unless the kidney was conserved, when it was marsupialized into the bladder to obviate the obstructive effects of the urethral sphincter.

Simple ligation and division of one ureter has often been practised in the past (Goldstein and Klotz, 1945), though not generally favoured (Campbell, 1951c; Higgins *et alii*, 1951b; Gross, 1953b), and in this series it has been performed four times. The corresponding kidney segment has not become infected subsequently and has not otherwise affected the patient's health adversely. The ligation was carried out at the upper end of the ureter in two children and at the lower end in one child. The two high ligations were done prior to the routine use of micturition cysto-urethrography, which now demonstrates post-operative reflux up the stump of these ureters (Fig. II). Prophylactic triple micturition is now carried out daily.

In one patient the ectopic ureter was heavily infected, the content being thick creamy pus. The ureter was drained by a flank ureterostomy for several weeks until the urine became clear. Successful ligation with cessation of symptoms was performed subsequently. We consider that both hemi-nephrectomy and ligation are inadvisable as primary measures in the presence of thick creamy pus. A preliminary period of ureterostomy drainage promotes regression of both the intrarenal and perirenal infection, after which either operation becomes simplified and safe.

The surgery of the derelict double ureter

Bilateral cases may appear derelict because of the severe combination of obstructive and idiopathic megaureters, because of ureteral reflux, and because of the lack of kidney parenchyma. But by the use of our special radiographic techniques, we have been able to ascertain in our several bilateral cases the presence of adequate renal function to permit appropriate surgery. Triple micturition training can then be applied to remove the reflux urine. By these means, the good and the bad kidney parenchyma are able to function under optimal conditions, and keep the children in satisfactory health.

Surgery of conjoined ureters

Here, as in vesico-ureteral reflux, the dominant symptoms are referable to infection.

This is caused by a reflux from ureter to ureter causing retention of urine. When the calibre of the ureters is normal reflux is small in amount; there may be only an occasional short attack of infection which can usually be cured by specific chemotherapy.

But when the conjoint ureters are abnormally large—megaureters—and the ureteric stem is only of normal calibre the urinary retention becomes so serious that surgical measures have to be adopted, as in two cases in our studies.

In one case, the megaureters and their corresponding renal segments down to the site of the junction with the normal ureter had to be removed to cure the child. And in the other case (Fig. IV), because the function of the renal segments corresponding to the megaureters was good, a special procedure had to be designed to save both segments. The common normal calibre ureteric stem to the

bladder was converted into a refluxing ureter by suprapubic uretero-vesical meatotomy. To do this the roof of the submucous course of the ureter was incised over a grooved probe, and the cut edges of ureter wall and vesical mucosa were oversewn. Following this plastic operation the ureter refluxed freely from the bladder. Triple micturition effectively empties the residual content (Fig. IVb). This recently introduced operation for removing the residual urine in these circumstances is still under trial. The child is in good health and the urine is free from pus.

FOLLOW UP

All the patients have been under regular observation for periods varying from eight months to nine years.

In 4 children unexplained recurrences of infection followed operations performed before micturition cysto-urethrography became routine practice in the investigation of suspected cases of double ureters.

Two of these children were found subsequently to exhibit free reflux up one or more ureters and hence to require further treatment. Triple micturition was instituted for one of them, and excision of the ueteral stump performed in the other. The infections in both were cleared up satisfactorily. We now consider that the management of the second of these children by triple micturition alone would have been sufficient.

In the third case, it would now appear that we removed in error the ectopic portion of the double kidney. It was subsequently necessary to resect the orthotopic portion. The diagnostic practice of micturition cysto-urethrography would have avoided this. Perhaps in this child, at least one, and probably two operations could have been avoided. Perhaps the kidneys could have been spared and infections satisfactorily dealt with by triple micturition.

The fourth case, a baby, died three months after hemi-nephrectomy. Urinary infection persisted together with a severe enteritis. The baby died at home and a necropsy was not performed. It is quite likely that in one or both the other ureters reflux caused persistence of the infection.

Two other children, making 6 altogether, were treated surgically prior to the use of micturition cysto-urethrography — one by excision of the double kidney and partial double ureterectomy; and the other by simple division and ligation of the ectopic ureter. Symptoms and signs of infection were arrested in both cases, and the urine remained sterile for two and one-half and five and one-quarter years respectively. When a follow up micturition cysto-urethrography was made the first child showed free reflux up the stump of one large ureter, and the second, free reflux up all three ureters, including the stump of the ligated ureter (Fig. II). This patient is being treated by prophylactic triple micturition.

The remaining 22 children have, when necessary, been given specific chemotherapy for any infection in the initial stages. To prevent any further attacks we have used the various methods of eliminating residual urine, both surgical and non-surgical, which we have described earlier. Twenty-one of these children are now free of infection and are leading healthy lives. One still exhibits pyuria.

Three of the 22 children suffering the effects of single or multiple ureteric reflux are maintained in good health by triple micturition alone.

Micturition cysto-urethrography has demonstrated that triple micturition is required as an essential form of therapy in 12 children in this series of twenty-eight. More radical and more frequent use of surgery would have obviated the need for triple micturition in only two of these cases. Micturition cysto-urethrography would have altered the line of treatment in 3, and probably 5 others, who were not investigated pre-operatively by this method.

CONCLUSIONS

Experience gained in five years' study of double ureter disease may be summarized as follows:—

1. The symptomatology of double ureter disease is better understood, the diagnosis is more accurate, and the treatment is more effective.
2. The full and persistent exploitation of triple micturition has not only facilitated diagnosis, but in addition has

proved highly efficient as a means of ensuring the evacuation of residual urine and forestalling the infection which supervened on ureteral reflux.

3. This double ureter study has shown that, more or less the whole urinary tract is adversely affected by the anatomical anomaly, and that treatment must be based on the recognition of this fact.
4. Idiopathic non-obstructive megaureter, one of the common anomalies, is considered to be a developmental enlargement of the ureteric buds rather than the result of obstruction.
5. Debilitation of the ureteral valve mechanism, also common in double ureter disease, is a further anomaly affecting ureters of small or large calibre.
6. It can now be accepted that the routine application of comprehensive cysto-urethrographic methods of examination more than any other single procedure, helps to uncover anatomical anomalies in the urinary tract and their associated disorders of function. Many of the disappointing results of treatment were shown to be due to lack of the knowledge which is now provided by this method of investigation. The guilty ureters in this disease are clearly pinpointed and appropriate treatment can be directed confidently and specifically to each one.
7. Finally, in general, our experiences in these studies suggest a definite trend towards conservatism and have engendered a confidence in treatment which is shared by both patient and doctor alike.

ACKNOWLEDGEMENTS

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I wish to thank the directors and all members of the Departments of Pathology, Radiology and Photography who have so kindly advised us and spent much time on the material submitted to them during the course and preparation of this work.

In the preparation of this paper both Sir Hugh Devine and Dr. Reginald Webster have afforded me much advice for which I am most grateful.

Finally, it must be acknowledged that without the assiduous and patient co-operation of parents in the training of these children, we could not have hoped to achieve these results.

ADDENDUM

Since this paper was completed, an excellent review of the subject "Ectopic Ureterocoele in Infants and Children" has been brought to my notice (Ericsson, N. O., 1954, *Acta Chir. Scand.*, Supplement 197).

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HIATUS HERNIA*

By F. W. Niesche

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As little has appeared in the Australian literature concerning hiatus hernia, it may be opportune to give experiences and impressions regarding its surgical treatment.

It is difficult to produce large figures in this country but now that over sixty patients have been treated surgically, I feel that an opinion may be justifiable.

In uncomplicated cases with definite symptoms, I have found that repair of the hernia gives excellent results and is one of the most satisfactory operations in surgery. By complicated types I mean those with permanent strictures and gross peri-oesophagitis and which are difficult to dilate, due to many years of reflux oesophagitis and ulceration.

FIG. I. Large para-oesophageal hernia. The inverted stomach lies above the diaphragm.

I am limiting my figures to cases done since 1951, when Allison clarified the types of hiatus hernia and described his method of treatment. All my patients have had their herniae repaired by a transthoracic approach using a modification of the repair as suggested originally by Allison. I consider that the views of Allison and Barrett are sound and that their methods give a good anatomical repair. My own opinion is that the transthoracic approach will meet all requirements and give a much better anatomical repair and fewer recurrences than by an abdominal route.

FIG. II. Lateral view of same case as in Fig. I. The oesophagus can be seen posterior to the stomach.

I am aware that most para-oesophageal herniae and many sliding mediastinal ones can be repaired quite well below the diaphragm but consider that the operation above

*These remarks are the basis of a paper read at a meeting arranged by the State Committee of the Royal Australasian College of Surgeons held in Sydney on 19th April, 1956.

the diaphragm can be done with more precision.

In many of the patients with reflux oesophagitis and much peri-oesophagitis and secondary shortening of the oesophagus, it would be impossible to do the operation below the diaphragm without injury to the oesophagus.

The dissection is sometimes extremely difficult and may entail freeing the oesophagus to a fairly high level to allow the cardio-oesophageal junction to be brought down below the diaphragm without any tension. Patients need to be selected carefully for an abdominal approach.

FIG. III. The repair is completed. Same case as in Figs. I and II. Taken following convalescence.

Essentially, the repair of sliding mediastinal herniae and para-oesophageal types, large and small, by the transthoracic route is the same.

After surveying the literature it appears that the recurrence rate in certain centres has been high and Wells (1955) states that it has been so prohibitive that he has abandoned the repair and advocates a partial gastrectomy and vagotomy and a Roux type of anastomosis with the jejunum.

FIG. IV. Girl aged 13 years. Shows a high level stricture.

This has not been my experience and the following are my own figures:—

Number of patients: 61. All treated surgically.

Females	40
Males	21
Total	61

Ages: 32-76 years. Two children 13 and 14 years.

Sliding mediastinal	40
Para-oesophageal	17
Mixed (predominantly para-oesophageal)	4
	61
Over 70 years	3
Over 60 and under 70 years	16

All have been referred by physicians on account of intolerable symptoms or failure with conservative treatment.

Mention may be made of five patients in particular.

1. A male aged 54 years had the complete stomach upside down in the chest (Figs. I, II and III).

2. A female patient, aged 62 years, had the whole stomach in the chest with some transverse colon and complete oesophageal obstruction. She arrived from the country being maintained with an intravenous drip. She had a very good convalescence following operation.
3. A female, aged 76 years, had more than two-thirds of the stomach in the chest and suffered intolerable symptoms. Her convalescence was quite satisfactory and she is very well after three years.

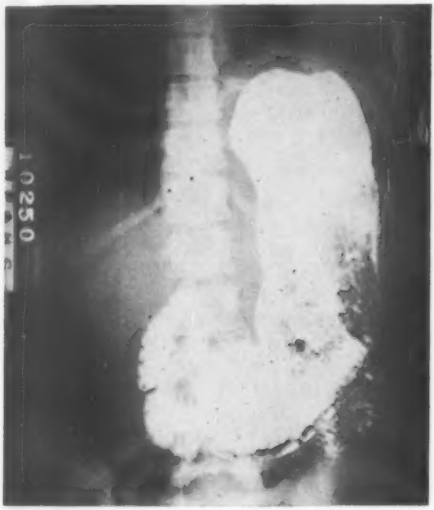

FIG. V. Same case as in Fig. IV following repair and taken during convalescence.

4. One male patient, aged 51 years, had a large penetrating ulcer in the thoracic portion of the stomach. He had a very large sac and the ulcer was adherent to the mediastinal tissues. This was freed and the hernia was reduced and repaired. He was placed on an ulcer regime. A subsequent X-ray taken a year later revealed no evidence of ulcer and no hernia. His operation was done in 1953 and he was symptomless when he reported very recently.
5. One patient, a female, aged 53 years, required a second repair for recurrence. The first operation had been performed by another surgeon elsewhere. She is well and has had no further recurrence.

Strictures

Eight patients had strictures. Four varied from mild to moderately severe but were easily dilatable. These have been satisfactory since repair of the hernia. One child aged 13 years, with the thoracic portion of the stomach at a high level, had dilatations periodically for six years at another hospital. Following extensive mobilization of the oesophagus, crushing of the phrenic nerve and repair of the hernia, she had a satisfactory result. A few dilatations were required subsequently (Figs. IV and V).

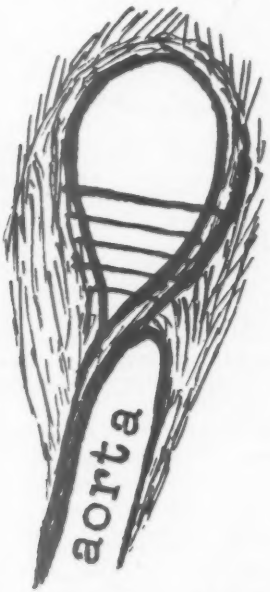

FIG. VI. Showing position of sutures inserted into the two portions of the right crus.

Four patients had severe strictures. Three had repair of the herniae. One patient, aged 45 years, maintains her weight with a liquid diet and has had several dilatations. She has been advised to have the stricture resected but is undecided as she is reasonably comfortable with liquid diet. The second patient, aged 67 years, is well following repair and careful dieting. She has had several dilatations and it is thought that she will not require resection. The third patient, aged 14 years, will require resection and she will be referred to subsequently. The fourth patient, a female aged 45 years, had a stricture which

was impossible to dilate and resection with a gastro-oesophageal anastomosis was done as a primary procedure.

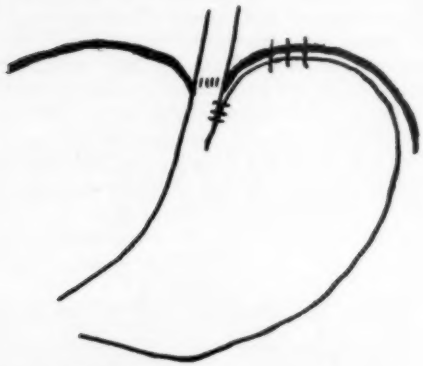

FIG. VII. Shows the formation of an abdominal oesophagus. Sutures are inserted between the oesophageal wall and hiatus, fundus and diaphragm and the oesophagus and fundus.

Gall-stones

Two patients had gall-stones. One had a cholecystectomy during convalescence following repair of his hernia and is now symptomless. One will require a cholecystectomy later if she has a recurrence of biliary colic. My impression is that a cholecystectomy should be advised when gall-stones are present with hiatus hernia. This can be done during convalescence following repair of the hernia or at a later date.

Duodenal ulcer

One patient, a male aged 54 years, who had a large penetrating duodenal ulcer, required a partial gastrectomy subsequently for massive haematemeses. He had no recurrence of hernia.

Deaths

In the whole series there was one post-operative death. He was a male aged 68 years, and died from a massive pulmonary embolus. Large varicose veins were present in both legs.

There have been several patients with a carcinoma at the cardio-oesophageal junction complicating hiatus hernia. These have been resected but are not included in this series. Invariably the radiological diagnosis was carcinoma in the middle to lower third of the oesophagus.

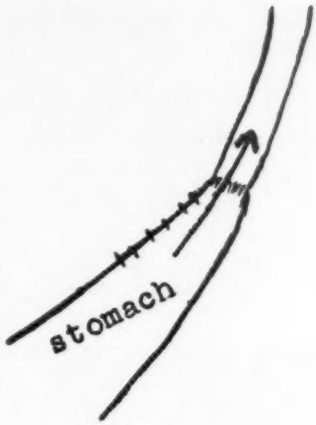

FIG. VIII. When the oesophagus is anastomosed to the proximal portion of the stomach there is no barrier to reflux.

Recurrences

Radiologically two patients have shown a small thoracic sac but both are symptomless. One, a male aged 46 years, is a harbour pilot and began climbing up the sides of vessels less than two months following his operation. Actually he states that he is very well and eats and drinks without restriction. Most likely he will have a return of symptoms.

FIG. IX. Following resection, the oesophagus is implanted low down into the portion of the stomach which lies above the diaphragm. Sutures are inserted between the oesophagus and fundus.

One female, aged 54 years, has symptoms of reflux but radiologically no recurrence of hernia can be demonstrated.

The child aged 14 years falls into a different category. I consider that she has a congenitally short oesophagus with a gross

stricture, and that the gastric pouch was never completely reduced. She may have gastric mucosa in the oesophagus as described by Barrett (1954). Her stricture should have been resected as a primary procedure. I feel that it was an error in judgment on my part and resection is being arranged.

With a recurrence, a para-oesophageal type of hernia may be converted into a sliding mediastinal one with its train of symptoms.

REPAIR

My impression is that the two cardinal procedures following reduction of the hernia are: (1) To close the gap between the two portions of the right crus of the diaphragm to prevent recurrence of the hernia, and (2) to reproduce the acute angle between the terminal oesophagus and the fundus of the stomach to prevent reflux of gastric juice.

OPERATION

A left transthoracic exposure is made through the eighth intercostal space. After incision of the mediastinal pleura, the oesophagus is mobilized well with the peritoneal sac. If necessary the lower aortic branches are ligated and cut to make sure that there is no tension on the oesophagus.

The diaphragm is incised and the peritoneal sac is distended by pushing several fingers up through the hiatus and the sac is cut away.

The two portions of the right crus are dissected free and well defined and particular attention is paid to the right part of the right crus. It is essential that the right portion of the right crus should be displayed clearly to enable the repair to be done with precision.

The hernia is reduced and interrupted sutures of chromic catgut are inserted between the two portions of the right crus to obliterate the large space but are tied later. Usually I allow the tips of the finger and thumb gauge the tightness of the closure. There should be some slight post-operative dysphagia (Fig. VI).

At least one inch of the oesophagus adjacent to the cardio-oesophageal junction is brought below the diaphragm. Fine interrupted sutures of chromic catgut are inserted directly into the oesophageal wall which is sutured to the sero-muscular edge of the hiatus. The oesophageal wall holds sutures well. This gives an abdominal oesophagus (Fig. VII).

Before closing the diaphragm a few interrupted sutures are inserted to fix the fundus of the stomach to the dome of the diaphragm and so reproduce the acute angle between the oesophagus and stomach. These have been inserted in all cases (Fig. VII).

A few interrupted sutures are also inserted between the oesophagus and the edge of the hiatus above the diaphragm after the large sutures are tied.

In my last two patients the oesophagus was sutured side by side to the fundus of the stomach and I feel that this may be an advantage.

Ulceration caused by reflux oesophagitis is shallow and usually heals following repair of the hernia. A large ulcer in the thoracic portion of the stomach will frequently heal after reduction of the hernia, or if necessary it can be excised. If resistant to an ulcer regime it can be dealt with below the diaphragm at a later date.

The patient with a stricture is the real problem. With those strictures which can be dilated easily I believe that it is justifiable to repair the hernia, particularly in the elderly. Once the reflux is interrupted, many strictures will subside and the patient may be comfortable with a few dilatations. If necessary resection can be done later.

I consider that the more permanent strictures will require resection. In some instances it is difficult to decide into which category a patient should be placed and this depends on personal experience.

Resection is a severe operation and the final method is controversial. Allison's method is very good but it cuts the stomach out of the circuit. The jejunum can be anastomosed to the oesophagus either as a loop or by the method of Roux. With my gastro-oesophageal anastomoses I have had little trouble and no obvious reflux as is so frequently reported.

I believe that anastomosis of the oesophagus to the end of the stomach is wrong in principle. There is no barrier to reflux of gastric juice, although with a higher anastomosis there is less tendency for regurgitation (Fig. VIII).

I consider that the oesophagus should be implanted lower down into the gastric remnant and the upper portion of the stomach sutured to the side of the oesophagus in an attempt to create an acute angle. The pouch above the anastomosis will tend to collect the juice when recumbent, particularly the resting juice (Fig. IX). Shaped like this and lying in the chest I believe that there will be little tendency to reflux oesophagitis.

Patients should be advised to reduce their weight and co-operation with a physician is most valuable. I cannot agree with a gloomy outlook and results indicate that repair of hiatus hernia is very satisfactory.

SUMMARY

The results of sixty-one cases of hiatus hernia have been presented. All have been treated surgically by a transthoracic approach.

One post-operative death is recorded due to a massive pulmonary embolus.

It is considered that repair of hiatus hernia is a very satisfactory operation and is justified by results and very few recurrences.

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MANAGEMENT OF HIATUS HERNIA

By Stanley Goulston

Sydney

THE diagnosis of hiatus hernia is now considered commonplace and with careful radiological technique is readily established. Harrington (1938, 1940, 1955) records that the earliest radiological diagnosis made at the Mayo Clinic was in 1921, but the condition was not generally recognized until very recent times. In the nineteen-thirties, ear, nose and throat surgeons, notably Clerf (1933), Manges, Findlay and Kelly (1931) reported cases of short oesophagus associated with thoracic stomach but they considered congenital oesophageal shortening to be the primary lesion. Great credit must be given to Harrington for his embryological studies and deductions and his understanding of the importance, symptomatology and management of the condition. His experience was profound, even in 1940, at a time when the condition was virtually unknown in this city. During the war and post-war years Allison (1951) and Johnstone (1955) popularized hiatal hernia and by careful observations demonstrated and emphasized the dramatic importance of reflux oesophagitis in the direct type of hernia with the attendant complications of ulceration and stricture formation. Barrett pointed out that the behaviour of an oesophageal ulcer depended on whether the oesophagus was lined with gastric or oesophageal mucosa.

During the past ten years many surgeons have reported series of cases operated upon for hiatus hernia, some advocating the thoracic, others the abdominal approach. There is still considerable difference of opinion as to the results obtained by each approach and method of repair.

Meanwhile physicians and surgeons became intensely interested in the so-called "cardiac sphincter" and the mechanism whereby reflux of gastric contents into the oesophagus is normally prevented. In this there is still wide diversity of opinion although there is general agreement on the mode of development of the herniae. The importance of these two factors — the manner in which the hernia develops and the way in which reflux is normally prevented are obviously vital to understand if surgical cure of a hernia is to be achieved and complications avoided.

Development of oesophageal hiatus hernia

Harrington regards the fundamental cause as being faulty embryological development. Delay in descent of the stomach and oesophagus results in imperfect development of the lumbar portions of the diaphragm and the oesophageal hiatus will be formed around the cardiac end of the stomach instead of around the oesophagus. This results in an abnormally enlarged hiatus with deficiency both in the muscle ring and in the attachments of the diaphragmatico-oesophageal ligament. This may give rise to symptoms at birth and the demonstration of a hernia, but generally herniation does not occur until the middle or late middle life when secondary factors, such as ageing tissues, obesity, pregnancy, chronically raised intra-abdominal pressure, trauma, ascites, pyloric stenosis, etc., act as the exciting cause. Occasionally herniae may be produced secondarily by primary oesophagitis or oesophageal cancer.

The prevention of reflux

Observations and experiments have been made by several workers. Prof. Johnstone, from his radiological observations considers the main factors in preventing reflux are—

(a) The oblique entry of the oesophagus into the stomach.

(b) Muscle fibres of the right crus.

(c) Sling fibres of the stomach (a band of fibres from the oblique muscle).

(d) Weak sphincter of the lower oesophagus.

Collis, Kelly and Wiley (1954) conducted an anatomical survey of 64 post-mortem specimens and concluded that the main action of the right crus (at times supported by the left crus) is to maintain the acute oesophageal entry at the cardia at all times but particularly during full inspiration. The action of

the right crus, they assert, balances the effect of the general diaphragmatic descent which would tend to aid reflux.

Other supporting evidence of the importance of the right crus comes from some experimental work at the Mayo Clinic. Guiseppi *et alii* (1954) produced oesophageal hiatus hernia by different means in dogs and found the most consistent reflux oesopnagitis occurred in those animals in which they destroyed the left crus (the left crus being the important muscle in the dog).

The great importance of the oblique entry of the oesophagus has been demonstrated in the United Kingdom by Marchand (1955). Using young male cadavers he clearly showed that by diminishing the oblique entry reflux is facilitated and by increasing it reflux is prevented. He also showed that in healthy male volunteers, reflux can be produced by increasing intragastric pressure using a rubber inflatable bag with a binder on the abdominal wall. He and many others believe that despite the lack of anatomical evidence there exists an intrinsic functional sphincter at the lower end of the oesophagus which is inhibited by swallowing at which time reflux may occur especially if the intragastric pressure is raised above the normal.

Dornhurst *et alii* (1954) used the technique of measuring oesophageal pressures in human volunteers with manometers through fine polythene tubes and as the result of their studies emphasize the importance of a so-called valve-like mechanism at the cardio-oesophageal junction, which they postulate is due to the mucosa and muscularis mucosa itself at this point. This valve, they consider, has little resistance to forward pressure but remarkably strong resistance to backward flow. This mechanism may explain the reflux associated with local gastritis, carminatives and emotion. Emotion may result in increased local vascularity and functional alteration in this valve-like mechanism.

In summary then, in the normal person reflux is normally prevented from occurring to any major extent (1) by the obliquity of entry of the oesophagus into the stomach maintained by supporting structures such as the liver tunnel, crura and surrounding organs; (2) by the intrinsic sphincter of the oesophagus, and (3) by a valve-like mechanism at the cardio-oesophageal junction. All these factors may be overcome by raising the intragastric pressure sufficiently high especially if swallowing should occur.

In the direct type, or sliding oesophageal hiatus heria, the normal oblique oesophageal entry is lost and reflux can readily occur. There is still a weak defence provided by the internal sphincter but any increase in gastric tension associated with postural change will cause reflux.

In any operation then for oesophageal hiatus hernia it is necessary to reduce the hernia and remove the sac, to prevent recurrence of the hernia by strengthening the supporting structures and to reconstitute and preserve the oblique entry of the oesophagus into the cardia.

Classification

Many different classifications have been presented, but fundamentally there appears to be two main types—

(a) Direct or sliding oesophageal hiatus hernia with elevation and displacement of the oesophagus.

(b) Indirect or rolling or para-oesophageal hiatus hernia, with normally situated oesophagus (although Johnstone maintains that in this type the cardia is always found above the hiatus), and maintenance of the oblique oesophageal entry.

There may be variants of these. One is described by Adams and Lobb of the Lahey Clinic (1954) as the oesophago-aortic variety where there is virtually a common opening and the sac will be displaced behind the heart. Combinations of (a) and (b) are not uncommon and such herniae are principally para-oesophageal.

I have personally examined the records at the Royal Prince Alfred Hospital, Sydney, and find that over the years 1951-1955 inclusive there were 121 patients admitted with a primary diagnosis of oesophageal hiatus hernia. I have not included patients with several diagnoses in which the hernia was not the main cause of the symptoms.

Of these 121 cases, 23 cases were of the para-oesophageal variety; 98 cases were of the

direct type, of which three had been present from birth and 95 acquired (Table 1).

TABLE 1

IN-PATIENTS, ROYAL PRINCE ALFRED HOSPITAL, 1951-55, WITH OESOPHAGEAL HIATUS HERNIA AS PRIMARY CAUSE OF ADMISSION

Total	121
Direct	98
Para	23

Symptomatology

The symptoms depend upon the type of hernia.

(a) The para-oesophageal hernia may be symptomless but may obstruct the oesophagus, become congested, an ulcer may form in it, or it may become strangulated. Consequently the symptoms are mainly those of attacks of vomiting, haemorrhage or pain. In this series of 23 cases of para-oesophageal hernia, nine had marked vomiting attacks due to pressure on the oesophagus, eight suffered considerable pain, and five had definite bleeding episodes. None suffered from reflux symptoms.

(b) The direct type is notable for the disturbing and unpleasant symptoms of reflux oesophagitis. There were 98 cases of direct oesophageal hernia in this series and of these 85 suffered from reflux oesophagitis of which 49 were severe. Of these 15 were shown radiologically to have some degree of stenosis.

Apart from reflux oesophagitis, 41 suffered from attacks of pain which appeared to arise from distention of the gastric pouch above the diaphragm or oesophageal spasm, and 24 had mild bleeding episodes which may or may not have been associated with the oesophagitis. It is my impression that severe haemorrhage does not occur with reflux oesophagitis and is usually due to some associated condition.

There was one case which conformed to the oesophago-aortic type with anginal type pain and vaso-vagal syncopal attacks.

Deaths

There were three deaths in this series. One patient died from rupture of an ulcer in the hernial sac, and one from strangulated hernia three months after its repair, and there was a post-operative death from a cerebral vascular accident.

Associated pathology

Seventy per cent. of this series had associated pathology in the gastro-intestinal tract, notably gastritis, gastric and duodenal ulceration, gall-bladder disease and cholelithiasis. The combination of oesophageal hiatus hernia, gall-stones, duodenal diverticula and colonic diverticula was frequently noted, and in addition coronary disease was common.

Investigations

When a diagnosis of oesophageal hiatus hernia is made, the following investigations are essential:—

1. A careful barium meal study to exclude peptic ulcer, etc. This will already have been done but if doubt exists it should be repeated.
2. Cholecystography.
3. Electrocardiography, including Master's exercise test.
4. Haematological study.

When this information is available a proper assessment of the patient's symptoms in relation to the hernia can usually be made.

In many cases oesophagoscopy is decidedly helpful in assessing the degree of oesophagitis and reflux and it is a useful pre-operative measure. In this series there were only 31 patients submitted to oesophagoscopy, about one-quarter of the total.

Management

When a definitive diagnosis of oesophageal hiatus hernia is made and the patient's symptoms can be fairly attributed to it, most patients can be managed reasonably well with conservative care. Most of those patients from the 50 to 70 age group are considerably overweight and reduction by several stones is often required. While this is well recognized by everyone it is rarely carried out and still more rarely maintained. It is also neglected by surgeons who, having repaired the hernia, fail to emphasize the need for continued dieting.

Advice to avoid sudden rises in intra-abdominal pressure, and to sleep with the

head of the bed raised, anti-cholinergic drugs and alkaline preparations complete the physician's armamentarium.

The need for surgery arises when complications such as uncontrollable reflux oesophagitis, stricture development, pressure phenomena, haemorrhage from the hernia, obstruction or attacks of severe pain are occurring. In my opinion there is no place for surgery in the uncomplicated case.

The management of this condition in infancy and childhood has its own peculiar problems which have been well recorded by Carré *et alii* in Birmingham (1952), and T. Y. Nelson of this city, but the principles remain the same.

Results of surgery in oesophageal hiatus hernia

If one studies the literature, one is struck by the lack of unanimity amongst surgeons regarding the cures obtained after surgical repair.

Harrington (Mayo), who appears to have the largest surgical experience and who generally uses the abdominal approach, records a recurrence rate of 2.8 per cent. in 450 repairs (operative mortality 1.3 per cent.), whereas Tanner of London (1955), using the same approach, found after only one year's follow-up almost a 15 per cent. recurrence rate (99 repairs, 73 completed one year, 67 traced, 41 satisfactory, 15 improved, and ten failures).

Sweet of Boston (1952), using the transthoracic approach, reports only 2 recurrences and no mortality in 108 cases, while Adams and Lobb found at the Lahey Clinic, using the same approach, a recurrence rate of 8.2 per cent after only six months follow-up in 59 cases.

Allison, using the thoracic approach, and operating on an undisclosed number of cases, reports a 10 per cent. recurrence rate.

Wells and Johnston stated in 1955 that the recurrence rate in their hands was so high that they no longer repaired the hernia and had resorted to gastrectomy and vagotomy.

In this series of 121 patients, 65 were submitted to operation at the hands of 12 surgeons. Of the 65 patients, 53 had a direct hernia and 12 a para-oesophageal hernia. These included three patients with post-operative recurrences from other hospitals.

I have personally attempted to review the 65 operated patients and 40 have attended the Clinic out of this number. No reply was obtained from 25 (Table 2).

TABLE 2

121 CASES OF OESOPHAGEAL HIATUS HERNIA, ROYAL PRINCE ALFRED HOSPITAL, 1951-55

Submitted to surgery	65
Direct	53
Para	12
Thoracic approach	58
Abdominal approach	7
Deaths	2 (3 per cent.)

The 40 were questioned and if their symptoms were suggestive of a recurrence they had a barium study performed. The results were as follows:—

Recurrences proved by X-ray	10
No X-ray recurrence but gross reflux radiologically	1
Severe operative sequelae	1
Severe symptoms without X-ray study performed	3
Severe symptoms with normal X-ray study	3

The X-ray recurrence rate in the 40 cases was 25 per cent. and the minimum rate for the whole group 15.4 per cent.

The unsatisfactory rate in the 40 cases was 45 per cent. and the minimum rate for the whole group 27.7 per cent (Table 3).

The time when the recurrences occurred after surgery are of interest. These occurred three years, three months, eight months, two weeks, three months, two years, six months, four years, one year, etc. When the recurrence occurred within weeks it seems obvious that the repair was at fault; those that recurred years later seem to be associated with considerable weight gain and inadvisable activity associated with sudden rises in intragastric pressure.

TABLE 3

65 OPERATIONS FOR OESOPHAGEAL HIATUS HERNIA, ROYAL PRINCE ALFRED HOSPITAL, 1951-56

Traced	40
Recurrences proved by X-ray	10
No X-ray recurrence but gross reflux	1
Severe operative sequelae	1
Severe symptoms without X-ray study	3
Severe symptoms with normal X-ray study	3
	18
X-ray recurrence rate, 40 cases	25 per cent.
And minimal rate for the whole	15.4 per cent.
Unsatisfactory rate in 40 cases	45 per cent.
And minimal rate for whole	27.7 per cent.

These facts have raised considerable doubt in my own mind that surgery is the final and easy answer to this problem. One factor that appeared obvious when reviewing these patients was the lack of supervision following operation with subsequent weight gain, often greater than the pre-operative level. These patients should be given definite instruction concerning diet and habits following operative repair.

In view of these findings one feels that operation should be reserved for complications and that conservative management as outlined should precede and continue after operation.

Finally, this review has made me realize that the physician should play a more active and definite part in the management of these cases.

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TETANUS AND THE ANAESTHETIST

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IT is nearly twenty-four centuries since Hippocrates first described tetanus and made the pronouncement that the severe case was always fatal — and it is only in the past three years that we have been able to take a more favourable view of this prognosis. The discovery of the causative organism by Nicolaier in the late 19th century, the concept of local infection by the organism and the central effects of the toxin, the development of active and passive immunization and the advent of antibiotics, all contributed relatively little to the management of the severe case of tetanus, although the incidence of the disease has decreased. Muscle relaxants, when first introduced, were used extensively in the treatment of tetanus but it soon became apparent that the overall mortality was not significantly reduced—the relief of the spasms meant that the patients suffered much less pain but they still died—chiefly of respiratory complications because adequate control of spasms was not possible without producing appreciable respiratory depression. As a result, the use of muscle relaxants as a therapeutic measure began to fall into disrepute and physicians were tending to revert to heavy sedation, combined with tracheotomy, while the mortality rate of severe tetanus still remained very high.

Ibsen and Lassen (1953) then introduced fundamental principles of anaesthesia into the management of respiratory paralysis. Their concept, in the treatment of any respiratory paralysis combined with bulbar palsy is early tracheotomy, adequate artificial ventilation and removal of bronchial secretions by posture and aspiration. In severe tetanus, full paralysing doses of relaxants are employed to control all spasms and thus the case becomes one of reversible bulbar palsy. Only a few reports on treatment by such means have been published but the results appear encouraging and it seems that tetanus can become a completely controllable disease.

This discussion is particularly concerned with the management of the severe case of tetanus and with details and complications of intermittent positive pressure respiration. The observations reported here are based on experience gained both at the Radcliffe Infirmary, Oxford, and the Royal Melbourne Hospital, in respiratory units for the treatment of cases of tetanus, poliomyelitis, acute polyneuritis, myasthenia gravis and severe head injuries, where the patients have required respiratory assistance for variable periods from twenty-four hours to seventeen days.

Pathogenesis

The disease is caused by local wound infection with the tetanus bacillus and the clinical picture is due to absorption of toxin, probably along peripheral nerves, and its fixation to anterior horn cells of the spinal cord and medulla. There the toxin produces irritation resulting in the two important clinical symptoms — muscle rigidity and reflex muscle spasms.

Clinical Varieties

Cole and Knott (1952) describe six varieties of clinical tetanus.

Type 1. Localized tetanus. The chief manifestation is localized muscle rigidity and the prognosis is good.

Type 2. Cephalic tetanus. In this form of localized tetanus the cranial nerves only are affected, most commonly the facial. Again, the prognosis is good.

Type 3. Tetanus with generalized tonic rigidity. Reflex spasms are slight or absent and prognosis is good.

Type 4. Tetanus with generalized tonic rigidity and reflex muscle spasms. This is the common form of severe tetanus and has a high mortality.

Type 5. Splanchnic tetanus. Deglutition and respiration are affected most and

generalized symptoms do not appear. It is said to follow visceral infection and, to date, has been extremely fatal.

Type 6. Infantile tetanus. Due to infection of the umbilical cord. It is a form of generalized tetanus but the tendency to convulsions is greater and there is a very high mortality.

From the point of view of modern therapy, however, the above classification is unnecessarily complicated. Cases of tetanus may be divided into two distinct groups.

1. The mild case. This is the case which exhibits local symptoms only or very slight generalized rigidity.
2. The severe case. Any case of tetanus which exhibits generalized rigidity, with or without reflex spasms, is a severe case of tetanus and requires intensive therapy. The severe cases may be subdivided into:
   (a) Cases with generalized rigidity with or without occasional spasms.
   (b) Cases with generalized rigidity and severe reflex spasms.

The therapy in these two groups is quite different.

CLINICAL DIAGNOSIS

The clinical picture of the severe case of tetanus is typical and usually presents little difficulty for diagnosis. The full picture is one of trismus, risus sardonicus, rigidity of abdominal wall and of limbs and limitation of respiratory excursion. Reflex spasms may result in dysphagia, laryngeal and bronchial spasm and severe respiratory embarrassment with consequent hypoxia and carbon dioxide retention.

The patient suffers severe pain with the spasms which, in the very severe case, are readily provoked by minor stimuli and may occur at very brief intervals. Mental faculties are quite unimpaired. The stage of spasms may last one to three weeks but rigidity will usually persist for much longer.

DIFFERENTIAL DIAGNOSIS

1. Trismus and dysphagia may suggest local infections of the throat — diptheria, peritonsillar abscess, infected molar tooth.
2. Spasms may suggest strychnine poisoning, rabies, tetany and meningitis.
3. Abdominal rigidity may result in the diagnosis of an acute abdominal catastrophe.

ASSESSMENT OF SEVERITY

It is important at an early stage to decide on the severity of the disease because on this depends the subsequent treatment. Three features are important in deciding the likely course of the disease:

1. The incubation period. This is often difficult to determine and unreliable but in general it is said that if the incubation period is more than seven days, the outlook should be good.
2. Period of onset. This is the interval between the first sign of rigidity and the first spasm and is much more reliable as a guide to prognosis. If the onset is more than three days the case is not likely to be severe. There are few reports of recovery where the period of onset is less than twenty-four hours.
3. Age. Patients over sixty and under three years of age tend to develop the more severe forms of the disease. Pre-existing disease will also affect the prognosis.

THE TREATMENT OF TETANUS

Teamwork.

This is one of the most important single factors in the management of any case of tetanus. The team should consist of a physician, anaesthetist and surgeon. In addition, ancilliary services including radiology, biochemistry, physiotherapy and bacteriology should be employed when necessary.

The team should see the patient as early as possible, should confer on the type of treatment that is necessary and should agree on any changes in management that may be required to suit the individual case.

I. Immediate treatment.

As soon as any case of tetanus has been diagnosed the immediate treatment should be:

(a) Control of reflex spasms. In the first instance a sedative should be administered,

preferably by intravenous or intramuscular injection. In the more severe case it may be necessary to administer a relaxant agent such as mephenesin as part of the immediate treatment. If the case is very severe on admission, then full curarization and intubation may be required as an emergency measure.

(b) Administration of anti-tetanic serum. When the patient has been adequately sedated, a skin test should be performed and 200.000 units of antitoxin administered by intravenous or intramuscular injection.

(c) Administration of antibiotics. At this early stage penicillin and streptomycin should be employed after swabs have been taken from the wound and from the sputum for culture and sensitivity tests.

(d) Observation. The above measures will halt the immediate progress of the disease. It is now necessary to observe carefully the effect of sedation and to be on the alert for the development of further spasms. It is extremely important to have at hand drugs and equipment for the immediate control of severe spasms, endotracheal intubation and ventilation of the lungs. Many cases are reported where the patient with apparently mild symptoms suddenly develops a severe spasm with respiratory embarrassment leading to death within a few minutes. There is no excuse for such a calamity in a properly equipped modern hospital.

II. Subsequent treatment.

Further treatment depends on the severity of the disease. In all cases the general principles of treatment are the same but the management from the anaesthetist's point of view is entirely different.

A. *Mild tetanus*

This is the common form of tetanus and the patient exhibits localized spasms or only moderate generalized rigidity. Although this type of case does not particularly concern the anaesthetist, he should observe it carefully in case more active treatment is required if the disease progresses.

(i) General management includes administration of A.T.S., treatment of the wound, antibiotics, careful nursing in quiet surroundings, attention to nutrition and fluid balance.

(ii) Sedation. Sedation without respiratory depression is essential. For this reason the opium alkaloids and allied substances should be avoided. Most satisfactory are the medium to long-acting barbiturates, e.g. pentobarbital, phenobarbitone, or paraldehyde and choral hydrate. Prolonged administration of large doses of barbiturates may lead to liver damage; therefore, it is advisable to vary the sedatives given every two to three days.

(iii) Careful observation to ensure that the disease does not progress to a more serious stage necessitating the administration of relaxants.

This type of case will usually resolve on the above regime in one to four weeks.

B. *Severe tetanus*

As mentioned earlier, the severe case of tetanus may be divided into two sub-groups.

(i) Moderately severe. The patient has generalized rigidity and reflex spasms of moderate severity which are provoked by definite stimuli. This patient may well progress to the more severe forms of the disease.

(ii) Very severe. This patient exhibits the full picture of tetanus with severe reflux spasms interfering particularly with respiration.

This subdivision is of considerable importance because, although the general principles of treatment are the same, the type of relaxant, sedative and pulmonary ventilation differ in the two groups.

1. The provision of an adequate airway.

This can usually only be ensured by early tracheotomy. A few cases of severe tetanus may survive with their own natural airway but the great majority must have an early tracheotomy if respiratory obstruction and severe pulmonary complications are to be avoided. In many cases reflex spasms become less severe and more easily controlled once tracheotomy has been performed, presumably because the hypoxic element in the spasm has been abolished.

Indications for tracheotomy in tetanus are:

(a) Respiratory obstruction.

(b) Respiratory muscle spasms, including laryngeal spasm.

(c) Dysphagia and trismus with pooling of pharyngeal secretions.

(d) Inability to cough adequately.

(e) Heavy sedation for long periods resulting in a semi-conscious patient with inadequate protective reflexes. A semi-conscious state and immobility for as short a period as twelve hours can result in severe respiratory tract infection — and indeed, most cases of severe tetanus have such an infection by the time tracheotomy has been performed. Hence the importance of early tracheotomy to enable adequate bronchial toilet.

Tracheotomy should never be an emergency procedure but should be performed in the operating theatre under endotracheal anaesthesia. Anaesthesia and a good airway provide ideal conditions for the surgeon to perform a leisurely tracheotomy without excessive bleeding and the danger of inhalation of blood. A high tracheotomy should be performed so that, if necessary, the patient can be nursed in a tank respirator. When the trachea is opened the endotracheal tube is removed while the surgeon inserts, for preference, a cuffed rubber tracheotomy tube.

At the same time, while the patient is anaesthetized, wound debridement and amputation, if necessary, should be performed, preferably by another surgeon. In addition a self-retaining catheter should be inserted into the bladder, a Rhefus tube passed and a cut-down intravenous drip commenced, if not already running.

By utilizing the anaesthesia for all operative interference at the one time, the patient is saved unnecessary stimulation.

2. Sedation.

Sedation should be as light as possible because all sedatives have a deleterious effect on bone marrow, liver and central nervous system. It is most important to avoid routine administration of sedatives because cumulative effects may occur.

Many sedatives may be employed but probably the best agents are the longer-acting barbiturates. Particularly valuable is pentobarbitone which can be given by intravenous injection in a dose of 0.25-0.75 gm. Intravenous thiopentone can also be employed but is short-acting, therefore a continuous infusion is necessary.

Paraldehyde is particularly useful in the less severe case and during convalescence. It should not be employed at the same time as intermittent positive pressure respiration because it is excreted by the lungs and therefore excretion may be delayed, pulmonary irritation may occur and, in addition, it is possible that paraldehyde may interact with soda lime.

Nitrous oxide would appear to be a most valuable sedative in the severe case. It is an analgesic and decreases, considerably, the amount of relaxants or other sedatives required. Until recently it was thought to be completely non-toxic but there is now some evidence that it may be the cause of bone marrow depression, seen in some cases of severe tetanus (Lassen, 1956).

3. Muscle relaxants.

Unfortunately there is no muscle relaxant which can completely relieve severe muscle spasms without also producing respiratory depression. Many of the reported cases of tetanus where relaxants have been employed, have died because of respiratory depression with all the consequences of hypoxia, hypercarbia and atalectasis. Therefore, if much relaxation is required it is necessary to fully curarize the patient and control respiration. The less severe spasms can, however, be controlled with mephenesin and the patient has two enormous advantages—he can breath for himself and has an adequate cough reflex. At all times, no matter what relaxant agent is used, there must always be the means of ventilating the lungs should any emergency arise. The following relaxants are employed in the treatment of tetanus:

(a) Mephenesin.

(i) For immediate relief of a spasm the 10 per cent. solution may be used intravenously in doses of 0.5-2 gms. This strength should only be used in an emergency.

(ii) For prolonged administration, continuous intravenous infusion is most effective. The rate of infusion can be varied according

to the spasms and excessive stimuli can be anticipated by increasing the rate of flow.

Concentration of solution should be not more than 2 per cent — it is usual to use 9-12 grams/litre. In twenty-four hours as much as 35 gms. has been used — but this is probably too much — if such a high dosage is being required then the patient should be fully curarized by other means.

(iii) Oral mephenesin may be used in very mild or convalescent cases. It is made up as an elixir—1 gram per half ounce. The elixir should be given via a Ryle's tube three to six hourly — in the more severe cases it may be given hourly. Patients receiving the elixir may need occasional supplementation with small intravenous doses.

Complications of mephenesin

1. Respiratory depression.

Although it is claimed that mephenesin is a relaxant which spares respiratory muscles, there is no doubt that, when employed in large doses, respiratory depression does occur.

2. Haemoglobinuria.

This is by far the most serious complication and deaths have been reported from renal failure, the pathological feature being intravascular haemolysis.

However, in all fatal cases the 10 per cent. solution was used and it is suggested that the complication is less common, and perhaps negligible, if less than a 2 per cent. solution is used (Pugh and Enderby, 1947).

At the same time daily urine examinations should be performed and if haemoglobinuria appears the drug should be stopped and another relaxant employed.

Recently a synthetic drug closely related to mephenesin (guaiacol glycerin ether) has been introduced and reports seem to substantiate the claim that it does not produce haemoglobinuria (Frey *et alii*, 1952).

3. Sedation.

Mephenesin tends to produce drowsiness due to a central sedative action, therefore care must be taken in the employment of other sedatives although these are still necessary.

4. Local anaesthetic action.

The elixir causes a marked analgesia and irritation of the mucous membranes. One death has been reported due to the inhalation of food associated with analgesia of the pharynx (Newhouse *et alii*, 1950). Therefore, it must never be given by mouth — especially if there is no tracheotomy. Even in the patient who has a tracheotomy it is safer to give it by Ryle's tube because the presence of the metal tracheotomy tube does not prevent aspiration of fluids and thin solids.

5. Venous thrombosis

Is due to irritating nature of the solution— this is less likely to occur if dilute solutions are used. But even so, the intravenous drips tend to stop due to thrombosis. This may be delayed by the employment of heparin 1000 units in each litre of intravenous fluid.

These complications of mephenesin are serious and therefore if it is necessary to employ very large doses another relaxant agent should be used.

(b) Continuous succinylcholine (Scoline).

Continuous intravenous infusion of the short-acting relaxant succinylcholine has been employed in a number of cases on the grounds that the rate of infusion can be modified according to the requirements of the patient (Woolmer and Cates, 1952; Forrester, 1954). With the concept of complete curarization and control of respiration, this drug has no advantage over the longer-acting agents as a slight overdosage at any stage is of little importance. Succinylcholine has less tendency to cause histamine release and bronchospasm than do other relaxants but, on the other hand, it does stimulate the production of bronchial secretions, patients occasionally become tolerant to the drug and the necessity of continuous infusion raises all the problems of supervision and interference with other intravenous therapy.

(c) Gallamine triethiodide (Flaxedil).

This agent requires to be given every twenty to thirty minutes and is reputed to have the advantages of little histamine release and ganglionic blocking activity. It also has less tendency to produce blocking of the intravenous drip and is compatible with most drugs.

On the other hand its short and often incomplete action is a disadvantage and the tendency to produce a tachycardia is undesirable when pulse rate is so important as a guide to pulmonary ventilation.

(d) d-Tubocurarine chloride (Tubarine).

This agent has longer and more complete curarizing activity than flaxedil and usually requires to be given every forty to one hundred and twenty minutes in intravenous doses of 5-15 mgms. With tubarine the pulse rate is slow, which is a decided advantage.

Tubarine does tend to produce a drop of blood pressure due to a ganglionic blocking action. It also has the reputation of causing bronchospasm. However, bronchospasm in tetanus is due to a number of factors and in most cases can be controlled by adequate doses of tubarine.

The use of depot tubarine in an oily base has been advocated by some but is rather variable in action and would appear to have little advantage over intravenous tubarine.

Decurarization

With the patient on complete curarization, it is necessary to decurarize at intervals to gauge the progress of the disease. However, the patient with severe tetanus suffers a serious setback each time he is decurarized and becomes quite difficult to control again. It may take up to four hours to control a patient who has had a test period without a relaxant agent. It is known, from the natural history of the disease, that spasms will certainly not pass off for three days and will probably last five to twenty-one days. No attempt at decurarization should be made for at least three days and thereafter it should not be done more than once every forty-eight hours.

During decurarization the respiration should be assisted by careful manual ventilation as this is the period when disordered respiration with all its dangers is most likely to occur. For this reason the anaesthetist in charge should undertake decurarization and the rest of the team should be present to observe the progress of the disease.

It is not recommended that prostigmine be used to antagonize the relaxant as the decurarization may be rather sudden, violent spasms may reappear and bronchospasm is likely to occur. The more tedious method of allowing the relaxant to be eliminated is the safest method. At the same time, some additional sedative should be given to make the whole process less violent.

If recurarization is necessary, it should be performed by a skilled anaesthetist who stays with the patient for some hours until full control is obtained.

Control of respiration

If curarization with any of the relaxant agents other than mephenesin is necessary, then it is essential to assist respiration. There are two main methods of applying artificial respiration — by means of a tank respirator or by means of intratracheal positive pressure respiration.

Tank respirators have the advantage of relative ease of operation and it is possible to leave the management of the respirator to a well-trained nurse. Improvements in the construction include special collars for patients with a tracheotomy and a device for producing an active expiratory cough impulse (Barach *et alii*, 1952).

On the other hand nursing is more difficult and it is necessary to take the patient out of the tank for adequate nursing care. During these periods it is usual to apply intratracheal positive pressure respiration. In a tank respirator it is difficult to assess clinically whether all areas of the lung are aerating adequately and spirometry is of doubtful value because compensatory emphysema may account for an apparently normal result. The chief disadvantage of a tank respirator, however, is that carbon dioxide retention can occur even though oxygenation appears satisfactory (Ibsen, 1954). Typically the patient appears a reasonable colour but is sweating and has a raised blood pressure. Pulmonary secretions and bronchospasm seem to be the main factors which render the tank respirator ineffective.

It was due to the high mortality of cases of bulbar poliomyelitis, nursed in tank and cuirasse respirators, that Lassen (1953) introduced, with dramatic results, intratracheal positive pressure respiration into the management of such cases. Subsequently he extended this regime to treatment of severe tetanus (Lassen *et alii*, 1954).

Intratracheal positive pressure respiration (I.P.P.R.) is employed constantly by anaesthetists for short term ventilation during anaesthesia. For long term respiratory resuscitation the chief disadvantage is the amount of skilled medical attention required. There are all the dangers of employing complicated anaesthetic equipment, wrong cylinders and exhausted soda lime. In addition correct methods of ventilation, so as to ensure adequate expansion of the lungs without hyperventilation or fall in cardiac output, are not readily learned, even by medical practitioners who are not trained anaesthetists.

On the other hand the advantages of I.P.P.R. appear to outweigh the above disadvantages. Adequate ventilation with elimination of carbon dioxide is ensured, nursing and physiotherapy procedures can easily be performed, it is possible to assess degree of curarization readily, pulmonary atalectasis can be recognized immediately and oedema of the lungs is counteracted.

Management of a patient on intratracheal positive pressure respiration

1. Situation.

The nursing of any case of tetanus requires a large special room with ample space for equipment and drugs. This applies particularly to the patient on I.P.P.R. There must be ample facilities for maintaining the sterility of intravenous injections, tracheotomy tubes and suction catheters which should be well separated from all trays dealing with bladder irrigation, feeding and other nursing procedures.

2. Personnel.

The management of I.P.P.R. should not be undertaken by nursing staff. For preference, only trained anaesthetists should supervise the ventilation throughout the twenty-four hours but, as this is not practicable, even in large units, it is important that an anaesthetist should be with the patient at periods which are likely to be difficult—after major manipulations, bronchoscopy, or decurarization. The anaesthetist in charge should spend at least six hours a day with the patient and must be the only person to make alterations in anaesthetic management—all other operators must abide by his decisions. Patients with tetanus have died because of divided control.

In general a four-hour shift is most satisfactory as it takes some time for an operator to get the "feel" of the patient. It is important that every operator should know the routine and any changes that have been made. The most convenient method is to write all details on a blackboard — including doses of drugs, times for posturing, physiotherapy and other procedures. In addition, the signs of hypoxia and carbon dioxide retention should be clearly written up so as to be before the attention of the operator at all times.

3. Equipment.

There must be available at all times a complete set of emergency equipment including oxygen, suction apparatus, laryngoscopes, bronchoscope, endotracheal and tracheotomy tubes. This equipment, in addition to a means of inflating the lungs, must be with every case of tetanus whether or not curarization and artificial respiration is being carried out.

For the purpose of intermittent positive pressure respiration either an absorber unit of the 'to and fro' or circle type can be employed or the patient can be ventilated by means of a semi-open circuit.

If absorption techniques are employed, management becomes more complicated because soda lime is involved. The patient on prolonged artificial respiration is a most sensitive indicator to rise in carbon dioxide tension and it has been found necessary to change the soda lime every hour — an expensive undertaking. On the other hand, if absorption techniques are used, humidification is not necessary. It is usual, although not essential, to employ absorption if nitrous oxide is being administered.

Open circuit techniques are probably more satisfactory because, although humidification is necessary, air or air enriched with oxygen can be employed and the equipment is less complicated.

A mechanical respirator is usually employed for prolonged I.P.P.R. but this does not abolish the necessity for the presence of a trained anaesthetist — indeed, the necessity is increased as the efficiency of any respirator depends on the ability of the person employing it.

There are many types of respirators available — none of them perfect. The main features necessary are simplicity, the correct cycle of respiration so as to avoid fall in cardiac output, and a release valve to avoid excessive pressures. The machine should be able to give some auditory or visual indication of excessive leakage from the circuit or of obstruction. It is also an advantage if negative pressure can be developed.

No mechanical machine is adequate if any complications develop such as pulmonary collapse or bronchospasm and, until such complications can be corrected, manual inflation must be employed.

Few machines will adjust themselves adequately to spontaneous respiration on the part of the patient, therefore, during test decurarization, manual inflation should also be used.

4. Management of the tracheostomy.

(a) Special tube.

A special cuffed rubber tracheotomy tube or cuffed endotracheal tube cut down to a suitable size is inserted in the trachea. After the first twenty-four hours there is no difficulty about inserting this tube but a set of sterile instruments, including tracheal dilators, forceps and retractors should be available. The cuffed tube should have the bevel cut off so as to decrease possibility of one lung anaesthesia and should be able to be adequately fixed to the neck. Care must be taken that the balloon is not over-inflated and it should be deflated for a period of thirty minutes twice a day. A brand new tube must be inserted every twenty-four hours. Deflation of the balloon and changing of the tube should be done with the patient in the head-down position and only after thorough suction of the pharynx.

Dangers of this tracheostomy tube are:

(i) Kinking—especially of portion projecting from the wound.

(ii) Obstruction—chiefly due to secretions and blood clot.

(iii) Over-inflation of the cuff causing protrusion of the balloon below tube.

(iv) Ulceration of trachea.

(v) Intubation of right lung due to excessive length.

(b) Aspiration of secretions.

This is done as often as is necessary but for preference should be performed just after patient has received doses of relaxant and sedative so that there is a minimum of disturbance to the patient. Suction should always be performed before and after changes in posture and physiotherapy.

Soft rubber catheters should be employed while Tiemans catheters and a Griffin's sucker should be used with great caution and only by people accustomed to their dangers. Absolute sterility is essential and excessive suction pressure should be avoided.

Bronchoscopy may be required if there develops any serious degree of pulmonary collapse.

Atropine is recommended by some people in order to decrease secretions. However, to a certain extent it renders the secretions more sticky and difficult to aspirate. In addition, it often causes an undesirable tachycardia. For the thinning and easy management of secretions in the trachea, dilute solutions of sodium bicarbonate are effective.

Alevaise or some other detergent can be nebulized and introduced into the circuit, although of doubtful value.

Pharyngeal and tracheal secretions are usually profuse and may be in part attributed to the presence of the rubber tube. Cuffed plastic tracheotomy tubes may overcome this disadvantage.

5. General nursing and physiotherapy.

These measures are most important and include care of the patient's pressure points, percussion of the chest and full limb movements. However, even more important to the patient are periods where he has no interference whatever. Therefore, all nursing and physiotherapy takes place at specified times, after additional doses of sedative and relaxant. The combination of suction, physiotherapy and posture is essential in the prevention of pulmonary complications.

6. Nutrition and fluid balance.

Intravenous therapy. A minimum of three litres a day is required. Excessive fluid loss should not occur in the properly managed patient but there will be increased loss from the respiratory tract.

Electrolytes. Attention should be paid to all the electrolytes and particularly to the danger of potassium depletion.

Blood. One or two pints of blood is useful in later stages.

Nutrition. High caloric fluids should be administered every hour through the Ryle's tube after aspiration — the usual amount is two ounces. The possibility of paralytic ileus must be borne in mind.

7. Detailed observations.

Apart from detailed progress notes by the medical attendants the following routine observations should be made:

(i) Blood pressure and pulse (half-hourly).

(ii) Temperature (four-hourly).

(iii) Times of administration of drugs.

(iv) Urine tests (daily)—
Red blood corpuscles.
Haemoglobinuria.
pH.
Albumin and chlorides.

(v) Chest X-ray — daily in early stages.

(vi) Blood (daily)—
Haemoglobin.
White blood corpuscles.
Red blood corpuscles.
Electrolytes.

COMPLICATIONS OF THE DISEASE AND THE TREATMENT

In text books the complications of tetanus are described as respiratory infection, secondary infection, dehydration, exhaustion and hyperthermia. The tetanus toxin itself does not appear to have any permanent effect. With modern methods of treatment most of these complications give little trouble.

Dehydration is corrected by intravenous therapy, secondary infection is prevented by antibiotics and exhaustion does not occur because the spasms are prevented and the patient receives adequate nutrition.

A. Respiratory complications.

These have been the chief cause of death in the past — due to a combination of excessive sedation, inadequate pulmonary ventilation, aspiration of secretions and food, poor nursing and lack of mobility. Even with a tracheotomy and adequate pulmonary inflation, respiratory problems give the main cause for concern and are frequently a complication of the treatment rather than the disease.

1. Inadequate respiratory exchange.

(a) Insufficient ventilation may be due to incorrect techniques of inflation, inattention, insufficient curarization, exhausted soda lime or leaks in the circuit.

(b) Respiratory obstruction may be mechanical, caused by kinking of the tracheotomy tube, over-inflation of the balloon or by blood and secretions.

Bronchospasm is one of the most difficult causes of obstruction. It may be due to the tetanic spasms, allergy to anti-tetanus serum or other drugs or to the presence of secretions. Adequate sedation and curarization and skilled attention are most effective in the prevention and treatment of bronchospasm. Occasionally anti-histamines and bronchodilators may be useful.

(c) Pulmonary collapse may be due to inhalation of secretions and blood caused by over-zealous manipulations of a suction catheter, to mechanical obstruction or to one lung ventilation if the tube is too long. Collapse is usually associated with some degree of infection which makes it more difficult to correct. Prevention and treatment consists of constant vigilance, antibiotics, physiotherapy, posture and aspiration of secretions and bronchoscopy, if required. A daily chest X-ray during the acute stages is extremely helpful.

2. Mediastinal emphysema.

This is caused by increase in intrapulmonary pressure, especially if there is also respiratory obstruction. It may occur due to excessive positive pressure or as a complication of tracheotomy. The air passes to the perivascular spaces into the hila of lungs and thence to the mediastinum causing compression of

pulmonary circulation. From mediastinum the air may go to root of neck, retroperitoneally or rupture through mediastinal pleura to produce a pneumothorax. The chief danger in I.P.P.R. is tension pneumothorax and interference with circulation in pulmonary tissue resulting in severe cyanosis. Pulmonary oedema may also occur. Mediastinal emphysema must be suspected if there is persisting cyanosis, difficulty in inflation and subcutaneous emphysema.

3. Hyperventilation.

Although hypoventilation is the commonest hazard of I.P.P.R., it is possible that a patient on prolonged ventilation may develop a low carbon dioxide tension — the chief effects of which are cerebral vasoconstriction and fall in blood pressure.

Blood pH estimations give the most reliable guide but are not readily available. Alveolar carbon dioxide tensions and serum bicarbonate estimations are of some assistance.

B. Hyperthermia.

This complication has, in the past, been ascribed partly to spasms and partly to central effects of the toxin. However, true hyperthermia does not appear to be a feature in a patient on I.P.P.R. and it is possibly due to a combination of spasms, carbon dioxide retention and cerebral oedema. Respiratory and other infections may play a minor part.

The possibility of hyperthermia should be remembered. It can be prevented by control of spasms, adequate ventilation, the head-up position and by not overheating the patient. Should hyperpyrexia develop, active cooling should be considered.

C. Complications of drugs employed.

(i) Serum reactions may result in allergic skin reactions which can be troublesome in maintaining the skin and in assessing hydration. Bronchospasm may also be a serious feature.

(ii) Haemolysis is a well-known complication of mephenesin and may lead to renal failure.

Heparin, often employed to prevent venous thrombosis, may also play a part.

(iii) Bone marrow depression.

Modern methods of treatment have resulted in the survival of an increasing number of cases of severe tetanus. At the same time there have appeared a number of reports of bone marrow depression (Lassen, 1953; Mollaret, 1955; Lassen, 1956). It was first suggested by Lassen that the relaxant agent may be responsible (Lassen, 1953). However Lassen (1956) has now produced some convincing evidence that nitrous oxide may be the causative agent. The present situation is that bone marrow depression does occur which may be manifest as a granulocytopaenia and thrombocytopaenia. This picture may be due to the tetanus toxin itself, barbiturates, relaxant agents, nitrous oxide or to the techniques associated with the administration of nitrous oxide.

Until there is more definite evidence, nitrous oxide and absorption techniques should be avoided but the relaxant agents and other drugs cannot yet be exonerated.

It is important that daily blood counts be performed and that the marrow be examined if the blood picture is suspicious of bone marrow depression.

D. Convalescence.

As mentioned earlier, it is necessary to test the progress of the diease at regular intervals by decurarization. A patient suffering from tetanus will not improve suddenly — usually after the seven to fourteen days the spasms become less severe and later still they are provoked only by severe stimuli. As the patient recovers further the spasms disappear completely and he is left with rigidity which will pass off over a period of two to four weeks. As the spasms decrease it is usually possible to decrease dose of relaxant but breaking off controlled respiration is difficult and experience shows that it is usually necessary to allow patient to breath spontaneously for gradually increasing periods and then to recurarize and control for a number of hours

as soon as there are signs of exhaustion such as a rise in blood pressure and pulse, sweating and tracheal tugging.

There will come a stage of improvement when mephenesin—either intravenous or oral will control spasms but not necessarily the rigidity and the patient must still be sedated. At the same time, during convalescence vigilance must not cease and equipment and drugs must be on hand at all times so that recurarization can be undertaken at a moment's notice.

CONCLUSIONS

1. Clinical tetanus is seen in mild and severe forms and the treatment of the two types is quite different. The management of the severe case has been described in detail in this presentation.
2. The general management of tetanus, including administration of antitoxin, antibiotics, intravenous therapy and wound debridement are more the concern of the physician and surgeon.
3. Sedation, relaxation and care of the respiratory functions are of vital concern to the anaesthetist.

   Sedation is best achieved by longer-acting barbiturates in minimum dosage.
   Relaxation is attained by mephenesin in the moderately severe case and in the very severe case, full curarization is obtained with d-tubocurarine, gallamine triethiodide or succinylcholine.

   Care of the respiratory system involves tracheotomy, physiotherapy, posture, aspiration of secretions and constant vigilance. If full curarization is necessary, artificial respiration is carried out by means of a tank respirator or by intratracheal positive pressure respiration. The latter method would appear more efficient.
4. Respiratory complications, while troublesome, should not be a cause of death.

   Bone marrow depression is a serious complication which is most likely to be due to one of the drugs employed. Once this temporary setback is overcome, there is no reason why the mortality from severe tetanus should not be abolished.

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PROLONGED CURARIZATION

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MOST anaesthetists have met cases of prolonged curarization of some degree. The causes to be considered on these occasions may be listed as follows: the administration of too much relaxant; synergisms with another drug — for example, Flaxedil and ether and succinylcholine and procaine; slow excretion of the relaxant as in cases with poor renal function; low plasma psuedocholinesterase levels and myasthenic conditions.

First, I wish to cite several case histories of patients suffering from symptoms of myasthenia gravis who remained curarized for many hours following moderate doses of relaxant. Later, other causes of prolonged curarization will be discussed.

CASE HISTORIES

Case 1

C.P., male, aged 36, weighing 10 stone, had a thoracotomy at the Alfred Hospital in March, 1952, and was found to have an inoperable carcinoma of the lung and died in the ward five hours later.

Anaesthetic: Thiopentone 0.5 gram and tubocurarine 30 milligrammes were given intravenously and maintenance was carried out with nitrous oxide and oxygen. No further injections of anaesthetic were given. The operation time was ninety minutes. Atropine 1/50 grain, followed ten minutes later by neostigmine 2.5 milligrammes, was given by intravenous injection at the end of the operation. After ten minutes respirations were poor and another 1/50 grain of atropine and 2.5 milligrammes of neostigmine were given. This so improved the patient's breathing that his colour was satisfactory while on nasal oxygen. However, the patient remained quite unrousable and at the end of an hour his respirations again became inadequate. His circulation, in general, was good all the time. Neostigmine and atropine in the same doses were repeated, following which the pulse became slow and weaker. Further atropine was given but the patient, still requiring artificial respiration, showed a steadily failing circulation and died several hours later having never recovered consciousness.

It should be stressed here that, at this stage, the reason for death was not obvious. Owing to the complete coma and lack of response to neostigmine except for temporary improvement after the first administration, it was considered that death resulted from some such cause as a cerebro-vascular accident or to hypersensitivity to one or other of the narcotic drugs. Autopsy gave no further information. It was not until the patient's out-patient card was found that the history was given that three years previously he had been in hospital complaining of weakness of the knees and ankles and blurred vision after prolonged reading, all of which improved with rest. The diagnosis of myasthenia gravis was considered possible although no definite improvement occurred with test doses of subcutaneous neostigmine at that time. We feel quite sure now that this patient suffered from myasthenia, although he was quite well in this respect at the pre-operative examination.

Case 2

A female patient, aged 31, weighing 9 stone 7 pounds, had a lobectomy performed at the Austin Hospital in March, 1954, for tuberculoma.

Anaesthetic: Thiopentone 0.4 grams and tubocurarine 25 milligrammes and maintenance with nitrous oxide and oxygen was used.

Hypotension was attempted with four doses of 20 milligrammes of hexamethonium but the blood pressure only dropped from 115 millimetres of mercury to 110 millimetres of mercury so that no further drugs were given throughout the operation lasting two hours. Ten minutes before the end of the operation, atropine 1/50 grain was given and then later 2.5 milligrammes of neostigmine were given. These were repeated later and the respiration improved sufficiently for extubation and the patient returned to the ward on nasal oxygen. She did not recover consciousness, her reflexes were absent, her pupils widely dilated, blood pressure 120/80 millimetres of mercury and pulse rate 80 per minute. Within two hours she had stopped breathing and she was intubated and given pulmonary ventilation by means of an anaesthetic machine with circle absorber. Allyl-nor-morphine 10 milligrammes were given intravenously as this appeared to be a narcotic coma but produced no improvement.

Several hours later it became known that she attended another hospital complaining of diplopia and weakness of her right thumb eighteen months before. On examination, the general findings were normal except for the ophthalmologist's report which stated that she had had weakness of her left superior and medial recti, that elevation of both eyes was poor, and diplopia was considered due to weakness of the left superior rectus. There was no record of any neostigmine test and the patient was discharged.

In view of this history, the possibility of prolonged curarization was considered and artificial respiration with regular changes of soda lime was continued throughout the night. Periods of apnoea were allowed occasionally in order to encourage the return of spontaneous respiration. However, this did not occur.

Next morning, 2.5 milligrammes of neostigmine were tried and consciousness dimly seemed to return temporarily but not the respirations.

That afternoon, twenty-four hours later, neostigmine 2.5 milligrammes were again given and respiration came strong enough for extubation, and regular does of neostigmine were then continued by mouth. Two days later, the patient became very weak again and fell out of bed but recovered after artificial respiration and more intravenous neostigmine. Thereafter, the patient recovered but her memory for the three days remained blank. She was later investigated at the Alfred Hospital, diagnosed as myasthenia gravis and stabilized on tablets of neostigmine and atropine.

Case 3

A male, aged 52, admitted in December, 1953, with muscular weakness of legs and arms for four months. One week before admission he noticed his voice was thick. On examination, he had slurred speech, wasting of the shoulder muscles, sternomastoids and trapezius, and the small muscles of the hands. No tongue wasting and no fasciculation was observed. All deep reflexes were absent.

Investigations

X-ray chest: Rounded mass regarded as carcinoma.

Muscle biopsy: Vastus lateralis was microscopically normal.

Response to prostigmine: Following injections of 2.5 milligrammes of neostigmine subcutaneously at different times, improvement of muscle power occurred. For example, after half an hour he could hold out his arms three times as long as before the test dose and he could sit up unaided.

Response to d-tubocurarine: Dr. R. H. Orton gave the patient 1 milligramme of tubarine intravenously. Prior to the injection each grip was 110 kilogrammes and straight leg raising from the bed could be prevented by one finger. Within two minutes the grip could not be recorded and he could barely move. The effect passed off in half an hour.

About this time, Anderson, Churchill Davidson and Richardson (1953) drew attention to the association of myasthenia gravis and pulmonary carcinoma and reported one patient in whom the muscle weakness cleared up following removal of the neoplasm. Pneumonectomy was therefore performed.

Anaesthetic: Pentothal 0.4 gram and slow intravenous injection of suxamethonium bromide (Brevadil M) was given and after 10 milligrammes the patient intubated and maintained easily for the duration of the operation with no further drugs. At the end of the operation, neostigmine was given, 1.25 milligrammes intravenously and 1.25 milligrammes intramuscularly.

Respiration returned to normal and the patient's condition was satisfactory until thirty-four hours later when the respirations became feeble and then stopped. Intubation and artificial respiration was started. Intravenous atropine 1/100 grain followed by 1.25 milligrammes neostigmine was given with improvement, the cough reflex, respiration and consciousness returned. The endotracheal tube was removed and intramuscular atropine and neostigmine given. One and three-quarter hours later the patient relapsed again, was intubated and restored with neostigmine. Again half an hour later the respirations ceased and again restored with neostigmine. Over the next half hour, despite artificial respiration, the patient's general condition deteriorated, pulse became irregular and death resulted. Autopsy was not allowed.

Case 4

A male, aged 48 years, was admitted on 1st March, 1955, complaining of weakness of legs for five months. Usually he was a good walker and was employed in the hill country destroying rabbits and wombats. From that day on he would feel weak in the legs at the end of the day. There was also a doubtful history of diplopia. His general examination revealed nothing unusual but the X-ray of the chest suggested a carcinoma and after further investigation, a thoracotomy was done and an inoperable carcinoma of the lung was found.

Anaesthetic: Pentothal — a sleeping dose, d-tubocurarine 45 milligrammes and a maintenance with nitrous oxide. At the end of the operation, respirations did not return, 2.5 milligrammes of neostigmine gave no result. Suspecting morphine sensitivity, allyl-nor-morphine 10 milligrammes were given intravenously without improvement. It was then decided to treat the patient as an unsuspected myasthenia gravis and to refrain from further drug administration. Artificial respiration with oxygen and an Aintree respirator for five hours followed when consciousness returned and the patient was able to maintain respiratory exchange.

He was then referred to the neurological department for investigation before discharge from hospital. The report stated knee and ankle jerks were weak, arm jerks absent and each hand grip below normal, being 170 kilogrammes. The right leg raising was good but the left leg very weak. One milligramme of d-tubocurarine was given intravenously. The left grip remained the same but the right grip fell to 140 kilogrammes. The left leg remained much the same but the right leg became very weak. After twelve minutes, 1.25 milligrammes neostigmine was given and in eight minutes each grip was 180 kilogrammes. A diagnosis of myasthenia gravis was made.

Case 5

D.H., male, aged 53, was admitted to the Royal Melbourne Hospital in June, 1955. For three months, he complained of weaknes in the legs after walking some distance. No abnormality of sensation was noticed. He also complained of a productive cough. On examination, he had wasting of the muscles of arms and legs, his sensation was normal, reflexes present and X-ray of chest showed a carcinoma of the lung. Bronchoscopy — was done twice under local anaesthesia and finally thoracotomy was performed and an inoperable carcinoma of the lung was found.

Anaesthetic: Pentothal 0.4 gram and d-tubocurarine 20 milligrammes with maintenance of nitrous oxide and oxygen. The operation time was two and a half hours, at the end of which the patient was still curarized. Three doses of neostigmine 2.5 milligrammes were given in the next hour with no help. He was sent back to the ward still attached to the anaesthetic machine and nineteen hours later, it was possible to remove his endotracheal tube. Five days later, at 4.30 a.m., he collapsed and died. Post-mortem examination showed widespread metastases including large masses in both supra-renal glands. Death was considered to be due to respiratory failure.

DISCUSSION

It can be seen that these cases all had symptoms of muscle weakness at some time before operation, but not necessarily at the time of the pre-operative examination; that is, the past history was significant.

In 1951, Churchill Davidson reported an investigation in which normal and myasthenic patients were given relaxants while conscious.

Response of myasthenic patients to depolarizing relaxants.

Using decamethonium to represent the depolarizing drugs, 2.5 milligrammes every two minutes were given intravenously. In normal subjects, a total dose of three milligrammes led to weakness sufficient to necessitate the cessation of further administration. In myasthenics, however, muscle action usually increased and was well sustained after doses totalling 10 milligrammes. Further administration led to paralysis appearing first in the muscles affected by the myasthenia. Thus, these patients showed a resistance to these drugs, but once relaxed remained so for a longer time.

Response to competitive inhibition type of drug.

Similar experiments show that myasthenics are very sensitive to d-tubocurarine. The muscles most affected by myasthenia are the more sensitive. Thus, if this is used as a clinical test on the conscious patient respiratory distress is unlikely to occur with the test dose of 1 milligramme.

Response to neostigmine.

In testing the response to neostigmine in these experiments the most notable discovery was that the prolonged paralysis resulting from the depolarizing drugs was relieved, while in fact it was expected to be increased. To explain this, it was suggested that the neuromuscular junction of the myasthenic patient responds in the same way as the monkey, dog and hare as shown by Zaimis (1952). She showed that, in these animals, decamethonium first produced a depolarization of the muscle and then later a competitive inhibition type of paralysis. This is known as a dual response. That is, the break-down products of the depolarizing drugs remain in the area and act as a competitor to acetylcholine. Also, animals who exhibit this dual response are less sensitive to the drug than those animals, such as the cat, who respond like the normal human being. That is, these depolarizing drugs, such as decamethonium, succinylcholine and Brevadil, are short-acting and potent drugs in the normal human or cat, but in the myasthenic human or monkey are weak and long-acting drugs and are reversible by neostigmine.

Association of bronchial carcinoma and myasthenia gravis.

It is clear that a percentage of patients who develop carcinoma of the lung also suffer symptoms similar to myasthenia gravis. Most of the cases cited above were of this nature and responded to relaxants in the same way as is expected of a myasthenic patient. The cause of this association is not understood.

Other factors in prolonged curarization.

As mentioned above, there are many factors associated with prolonged curarization. For example, Joske, Ebeling and Stanistreet (1954) reported four cases of what they called post-operative re-curarization. All these cases were given quite large doses of Flaxedil during the operation and neostigmine at the end. Apparently, the neostigmine was metabolized before the Flaxedil and the curarization returned and in two cases death resulted. They suggested that poor renal function may have caused the slow excretion of Flaxedil as it is not broken down in the body but largely excreted unchanged in the urine. Also, it must be remembered that poor renal function may be seen in patients with normal kidneys; for example in times of dehydration or shock.

Many cases are reported of prolonged apnoea following administration of succinylcholine. Most of these seem to have occurred

administration of mixtures of relaxants. For example, the use of the short-acting drug to after large doses have been used or following close the peritoneum when d-tubocurarine has been used for several hours. Succinylcholine is broken down in two stages—first to monocholine and then a slower process to succinic acid and choline. The monocholine is a weak relaxant and has no effect in ordinary circumstances but, owing to its slow metabolism, may accumulate to significant amounts in cases of large single doses. A low psuedo-cholinesterase level in the plasma may explain some cases after prolonged dosage. Bourne (1953) reported a case of a healthy girl who, on several occasions, remained in apnoea for three to four hours from a dose of 100 milligrammes of succinylcholine. Her pseudo-cholinesterase level was taken pre- and post-operatively and was at all times very low (17-21 units). Many examples have been shown since. However, as Orton has shown, psuedo-cholinesterase levels are not reliable on poor risk, apnoeic or anoxic patients as these conditions in themselves may lower the psuedo-cholinesterase level. In his investigations he was unable to show any relation between a psuedo-cholinesterase level and the amount of succinylcholine necessary to produce a given relaxation.

However, the cases of prolonged curarization in myasthenics have followed quite small doses of succinylcholine. Anderson, Churchill Davidson and Richardson (1953) carried out tests on a patient who, following administration of succinylcholine 50 milligrammes and pentothal 0.5 gram for a bronchoscopy, remained in apnoea for one and a half hours. The patient was a man of 47 years who complained of progressive muscular weakness—for example, he had to hold his head up while watching television and also suffered from transient diplopia and some hoarseness of his voice. The X-ray of his chest showed possible carcinoma of the lung. While the patient was in apnoea they did the following tests: Direct stimulation of muscle gave a normal response but electro-stimulation of the ulnar nerve showed a neuro-muscular block. This excluded a more central cause. Pseudo-cholinesterase was within normal limits — 50-120 units. Later, with the patient conscious they tested as follows:—

(a) Response to decamethonium: Two milligrammes of decamethonium caused paralysis of the body and severe respiratory embarrassment. One minute later, 20 milligrammes of Tensilon (a short-acting neostigmine analogue) returned the patient to normal.

(b) Response to d-tubocurarine: 3.75 milligrammes d-tubocurarine gave apnoea for twelve minutes.

(c) Response to succinylcholine: 7.5 milligrammes succinylcholine produced apnoea for six minutes. Repeating this, injection of 20 milligrammes of Tensilon led to immediate recovery.

(d) Response to neostigmine: The patient was given 15 milligrammes of neostigmine a day orally and his muscle weakness and hoarseness improved.

The complete coma in these myasthenic patients suggests a similar action to the unconsciousness produced by very large doses of tubarine. That is, the conduction through the synapse is affected in both these instances. This coma tends to mask the real condition of prolonged curarization.

CONCLUSIONS

1. There seems no relation between the severity of the myasthenia and the sensitivity of the patient to relaxant drugs. Myasthenia may be sub-clinical at the time of operation and yet the response to relaxants results in death of the patient.
2. The cases described did not have a typical appearance of prolonged curarization but rather of a deep central narcosis. Two cases would have remained mis-diagnosed but for the previous history of muscle weakness.
3. The association of bronchial carcinoma is sufficient to warrant a careful enquiry before anaesthesia. Incidentally, any patient with recent onset of myasthenia should have a chest X-ray.
4. If present with such a case of long post-operative curarization and the facilities are present, the following procedure seems indicated. Motor nerve may be stimulated electrically to reveal whether

or not the neuro-muscular junction is functioning or whether it is a case of central depression from the anaesthetic. Blood samples may be taken for the estimation of carbon dioxide retention and plasma pseudo-cholinesterase level. If a competitive inhibition type of drug has been used, neostigmine is given but, if only a slight or no improvement occurs, the patient is better kept ventilated and neostigmine not tried again until some hours later and then using small doses. There is no doubt that some deaths have been the result of neostigmine overdosage. If a depolarizing drug has been given then a careful trial with the short-acting Tensilon 10 milligrammes is indicated. If this produces improvement then ordinary dosage of neostigmine may be used in the treatment.

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ALVEOLAR SOFT PART SARCOMA

By JOHN V. HURLEY

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IF a group of neoplasms possesses characteristics of form or behaviour clearly distinct from other tumours occurring in the same region, its description as a separate entity is justified. Such a group of tumours found predominantly in or closely related to skeletal muscle was described by Christopherson, Foote and Stewart in 1952 under the title of "Alveolar Soft Part Sarcoma." Similar tumours have been reported previously under a variety of names, but the characteristics and behaviour of the group are not yet widely recognized nor is there any agreement regarding their tissue of origin.

This paper reviews briefly the previous literature, describes three further cases and considers the diagnosis and possible histogenesis of these tumours.

PREVIOUS LITERATURE

Christopherson, Foote and Stewart's group of 12 tumours had no striking macroscopic features but showed a very characteristic histological appearance of "pseudo-alveolar or organoid" arrangement of cells, quite distinct from any other tumour type found in association with skeletal muscle. They stated that the condition was unrecognized by a conference of American pathologists in 1946, and coined the name alveolar soft part sarcoma for the condition.

From a search of the literature, and in some cases re-study of the original slides, they identified cases reported by Ackerman and Phelps (1946), Klemperer (1934), Horn and Stout (1943) and Khanolkar (1947) as of the same nature, these having been described originally as myoblastoma, malignant myoblastoma, or rhabdomyosarcoma.

They further stated that they had no certain opinion regarding the histogenesis of the tumour but noted a structural resemblance to tumours of the carotid body and allied chemoreceptors.

In the previous year Smetana and Scott (1951) described 14 cases which, from their illustrations, are clearly identical with those of Christopherson *et alii*. Like these authors they found that approximately half the tumours became frankly malignant with multiple metastases. On the sole basis of a personal communication from Johnson, of the supposed presence of tissue resembling the carotid body in the femoral canal in one instance, they identified their tumours with those arising in chemoreceptor organs and named them malignant tumours of non-chromaffin paraganglia.

Subsequent single cases have been recorded by Randall and Walter (1954) and Hicks and Leitch (1955), and Willis (1953) states he has seen 5 cases of this type. All three agree as to their probable origin from chemoreceptor tissue.

PRESENT CASES

Case 1

T.S., a female aged 21 years, presented on October, 1949, with the history of a lump that had been present for six years on the lateral aspect of the left thigh and slowly increasing in size. She complained of no symptoms relative to the lump.

On examination a soft rounded tumour, roughly 6 cm. across, was found in the substance of the vastus lateralis. The tumour was soft but not fluctuant and a provisional diagnosis of intramuscular lipoma was made. The patient was operated on the next day and a firm, white mass embedded in muscle was found and removed together with a little surrounding muscle. Recovery was uneventful and the patient was known to have been well five years after the operation when trace of her was lost.

Biopsy specimen

A tumour measuring 7.5 x 7.5 x 5 cm. is embedded in skeletal muscle (Fig. 1). The tumour is macroscopically encapsulated and the cut surface is white in colour with scattered areas of haemorrhage and softening.

Histological examination

The tumour presents a remarkably uniform appearance throughout and is composed of polyhedral cells with abundant eosinophilic cytoplasm and relatively small inactive vesicular nuclei. In some cells cytoplasmic vacuoles are a prominent feature.

The cells are arranged in groups separated by capillaries and fine reticular fibres to produce an 'organoid" appearance. In many areas the central cells of such groups are absent and a "psuedo-alveolar" appearance results. Mitotic figures are not seen in any appreciable number despite careful search.

Reticulin staining demonstrates fine fibrils surrounding alveoli but not penetrating between individual cells. In sections stained by Palmgren's (1948) method nerve fibres could not be demonstrated in the tumour substance.

FIG. I. Photograph of cut surface of the tumour in Case 1 showing generally white surface with areas of haemorrhage and necrosis. Note the apparent encapsulation of the tumour.

Case 2

F.N., a male station hand aged 32 years, was kicked by a sheep in January, 1949, in the region of the left elbow. A haematoma developed which was evacuated by his local doctor.

Two months later in April, 1949, he presented with a lump 5 cm. across on the flexor aspect of the left forearm just below the elbow which was pulsatile and obviously extremely vascular. Operation at this time revealed two vascular tumours 7.5 x 6 cm. and 2 x 1.5 cm. respectively in the left forearm superficial to but infiltrating into the flexor muscles just below the elbow. A clinical diagnosis of sarcoma was made and a wide local excision carried out.

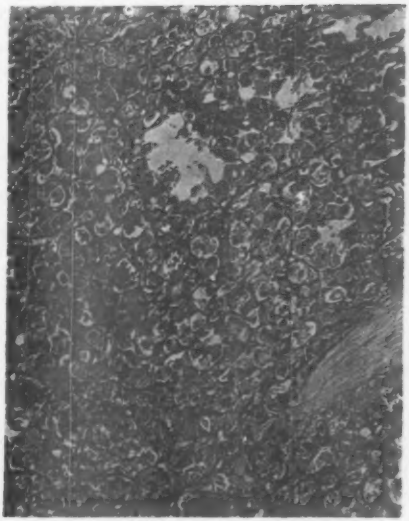

FIG. II. Photomicrograph of portion of tumour in Case 1 showing "organoid" arrangement of cells with abundant cytoplasm and small dark nuclei. Note the general resemblance to an epithelial tumour. Haematoxylin and eosin. (x 60)

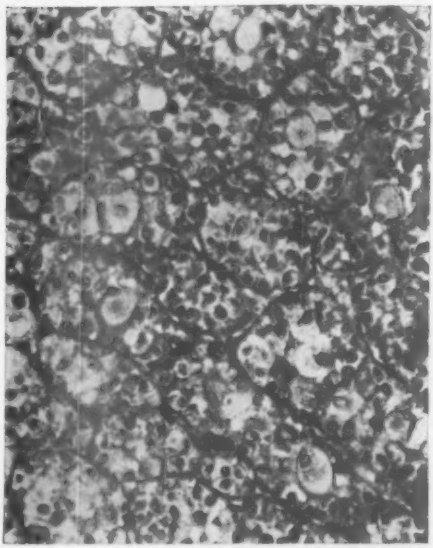

FIG. III. Photomicrograph of portion of tumour in Case 2 showing "pseudo-alveolar" structure of groups of cells surrounded by thin bands of reticulin fibres and blood vessels. Reticulin stain. (x 60)

Healing was uneventful but five weeks later on 1st June, 1949, a swelling 9 x 4.5 cm. was found to occupy the upper two-thirds of the anterior surface of the left forearm and a lymph node 2.5 x 3 cm. was palpated in the left axilla.

Deep X-ray therapy was given and over the next four months the mass did not increase in size but chest X-rays in May, 1950, that is, one year after operation, revealed multiple secondary deposits in the lungs. These were treated further with deep X-ray and decreased somewhat in size but two years later in June, 1952, they were enlarging again and further deposits were detected in the bones of the pelvis. Two months later the patient complained of pain in the left elbow and X-ray revealed a secondary tumour in the olecranon with a pathological fracture of the left ulna. These deposits were treated with X-ray but the patient's general condition deteriorated and he died late in 1952. No autopsy was performed but the left arm was available for examination.

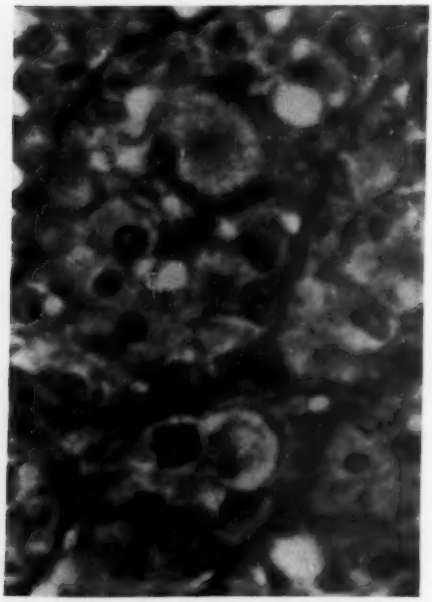

FIG. IV. Higher power photomicrograph of portion of tumour from Case 2 showing detail of cells with abundant cytoplasm and small inactive nuclei. Note "pseudo-alveolar" arrangement of cells. Reticulin stain. (x 200)

Biopsy report

The macroscopic appearance of the tumour was as in the operation report.

Histologically the appearance was almost identical with that seen in Case 1 — the same organoid or pseudo-alveolar arrangement of clear eosinophilic cells with inactive looking nuclei with reticulin fibres and thin-walled blood vessels between the cell groups. In this case a frozen section was examined and no fat was detected. In addition one or two small areas show groups of tumour cells lying within blood vessels.

Examination of the arm—post-mortem

Macroscopically an irregular whitish mass, 4 cm. in diameter and not encapsulated, lay in the muscles of the anterior and medial aspects of the elbow. The mass contained much fibrous tissue, and extended into the ulna which showed a transverse fracture across the base of the olecranon.

Histologically the material showed considerable autolysis and cellular detail was not good. The general arrangement was very similar to that of the primary growth, the cells being of the same form and general arrangement. However, considerable dense fibrous tissue surrounded the tumour and separated it from surrounding muscle and also subdivided the tumour tissue by coarse bands.

DIAGNOSIS

The first, and most important, problem, regarding these tumours is their histological recognition. With experience of them they form a readily recognized entity. If they are to be confused with other primary neoplasms occurring in muscle, the usual mistake has been to diagnose myoblastoma and, as previously mentioned, a number of cases has been described under this title. However, the characteristic coarse granularity of the cells of myoblastoma is absent and myoblastoma never shows the organoid appearance which is so striking a feature of alveolar soft part sarcoma. There is no real resemblance to the other common tumours of muscle—fibrosarcoma, spindle-celled sarcoma or rhabdomyosarcoma (Stout, 1946; Hurley, 1954).

A much more likely mistake is to diagnose a tumour of this type as a secondary carcinoma in muscle. The organoid appearance of large polyhedral cells often with relatively clear cytoplasm may strikingly resemble some epithelial tumours, notably carcinoma of the kidney or adrenal. It is probable that an error of this kind was made in the following case.

A.F., a girl aged 9 years, complained of a lump in the left triceps present for a month and increasing in size. On examination a mass 6 x 4 cm. was present in the posterior belly of the left triceps not fixed to skin or bone.

At operation the tumour was diffuse and ill-defined with infiltration of the superficial part of the muscle but more circumscribed on its deep aspect.

Histological examination revealed "masses of cells with clear cytoplasm and hyperchromatic nuclei arranged in columns. A moderate number of mitoses

are present and the tumour is seen to be invading muscle.

The growth is a secondary carcinoma and the appearance strongly suggests a primary in the kidney."

Subsequent intravenous pyleogram revealed no abnormality of the kidneys and a course of deep X-ray therapy was given to the left arm. Over the next seven years the child has remained well and grown normally with no signs of recurrent tumour.

Review of this case makes it almost certain that the histological diagnosis was mistaken as survival for seven years in perfect health with no treatment of the supposed primary is most unlikely. The sections of the original biopsy are technically unsatisfactory, but reveal an appearance closely resembling alveolar soft part sarcoma and this is now regarded as the most likely diagnosis, though the sections are not sufficiently good to make this opinion certain.

These two possible mistakes in diagnosis —myoblastoma and secondary carcinoma, assume greater importance when the life history of these conditions is considered. Myoblastoma is almost invariably a benign lesion, only 7 cases of malignant myoblastoma having been recorded (Ross, Miller and Foote, 1952).

Carcinoma presenting as a secondary metastasis in muscle has a uniformly poor prognosis, whilst the behaviour of alveolar soft part sarcoma seems to lie midway between these two extremes.

Of the cases so far on record Smetana and Scott have 10 cases followed up with metastasis in 9 and death in 5. Christopherson and Foote state that of 10 cases adequately followed, 6 developed metastases and 4 of these have since died, while 4 have remained well over a period of from five to fifteen years. In one case metastasis occurred eighteen years after the removal of the primary tumour. The two cases recorded here are thus typical of the larger group — one recurred rapidly and the patient died with generalized spread, whilst the other patient has remained free of recurrence for seven years.

It seems that in roughly half of the cases of this tumour recurrence is to be expected but that adequate local excision may cure the rest: this would appear, therefore, to be the logical treatment. The effect of deep X-ray therapy is in doubt. In the literature there is little evidence of its value, and in these present cases undoubted shrinkage of the lung secondaries occurred in Case 2, without preventing the final outcome. It may have played a part in the apparent "cure" in Case 3. Until further evidence is available it would appear that deep X-ray therapy may afford help and should be employed in addition to local excision.

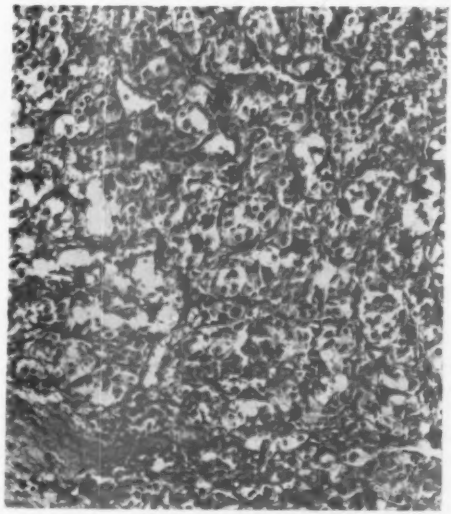

FIG. V. Photomicrograph of portion of a carotid body tumour. Selected as showing the closest resemblance to alveolar soft part sarcoma. Note the less regular arrangement of the cells. Haematoxylin and eosin. (x 60)

HISTOGENESIS

The final problem is whether or not these tumours are to be regarded as related histogenetically to the chemodectoma group—that is, tumours arising in the carotid body or related structures. Smetana and Scott first made this suggestion and Randall and Walter, Willis, and Hicks and Leitch have all agreed with it, without however advancing any more real evidence in its favour. Christopherson and Foote note the resemblance in appearance to some tumours of the carotid body but feel unable to classify these tumours, and quote Masson as being of the same opinion.

The evidence in favour of a chemoreceptor origin consists of two parts: first, the claimed histological resemblance to tumours of this system, and secondly a report of the presence of tissue resembling the carotid body in the region of the femoral artery by Johnson (quoted by Smetana and Scott, 1951). A further personal communication from Johnson adds the following information. In a search of blocks from infants by serial section he states that he "can almost always get the organs in the coeliac plexus, have occasionally seen them in the hilum of the kidney and only once have I been successful in finding one in the lower part of Hunter's canal." Smetana and Scott published a photomicrograph of this one case but it is not convincing.

Thus, whilst this work may be significant, in the absence of further confirmation it would not seem to offer alone sufficient basis for the supposed histogenesis of these tumours.

With regard to the histological resemblance, this group of tumours has been studied over some years in this Department by Birrell (1952) and careful study of his material fails to convice either him or the present author that the resemblance is at all a close one. Figs. V and VI represent the usual appearance of carotid body tumours for comparison with the tumours described in this paper. The main points of distinction are two: first, the carotid body tumour shows characteristic variation in pattern from one area to another, in contrast to the strikingly uniform picture of alveolar sort part sarcoma. Secondly, even in those limited areas of a carotid body tumour that superficially resemble the other tumour, the cells are much smaller. Thus Fig. VI, the high power photomicrograph of a carotid body tumour, resembles much more closely Figs. II and III, the low power view of the tumour in Case 1, than it does the photomicrograph of the same magnification (Fig. IV). Tumours of other undoubted chemoreceptor organs such as the jugular or vagal bodies are identical in appearance with those of the carotid body.

In addition to this paucity of evidence for the relation of these tumours to the carotid body group, there are certain observations against such an origin. First, careful staining of these tumours for nerve fibres by Palmgren's method has failed to reveal any nerves in the tumour substance, although nerves in considerable numbers may be demonstrated in both the normal carotid body and its tumour (Birrell, 1952; Willis and Birrell, 1955). Secondly, the behaviour of this group of tumours is quite unlike any other tumour arising in chemoreceptors. These are almost invariably benign in course although they may be locally destructive in character. Only 8 tumours of this group are on record as causing undoubted metastasis (Romanski, 1953). By contrast, in the relatively small group of alveolar soft part sarcomas, at least half have been frankly malignant with widespread metastasis.

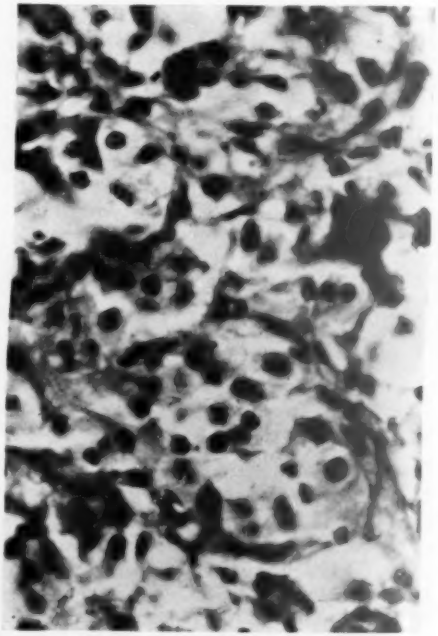

FIG. VI. Higher power photomicrograph of portion of the area shown in Fix. V. Note the smaller size of the cells than those of alveolar soft part sarcoma, and also the relatively larger nuclei. Haematoxylin and eosin. (x 200)

Considering all these factors the author is of the opinion that there is considerably more evidence against the possible origin of these tumours from chemoreceptor tissue than there is in favour of such an origin, and that until more evidence is forthcoming the histogenesis of these tumours is best re-

garded as unknown. Despite this they form a readily recognizable and distinctive group of characteristic behaviour and thus of clinical importance.

SUMMARY

1. The literature on alveolar soft part sarcoma —a distinct and recently recognized tumour arising in association with skeletal muscle, is reviewed.
2. Three new cases are recorded, and their clinical and pathological features are described.
3. The differential diagnosis of the tumour is discussed, with especial reference to its separation from secondary carcinoma.
4. The evidence for the histogenesis of the tumour is outlined, and it is concluded that it bears no relation to tumours arising in chemoreceptor tissue such as the carotid body.

ACKNOWLEDGEMENTS

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SARCOMA IN A FAMILY

A CASE REPORT

By R. M. Dunn and T. J. Constance

Sydney

A GOOD deal of information exists about the incidence of familial tumours in man. Most frequent examples are of carcinoma and valuable accounts include those by Waller and Wassink, and are discussed by Blank (1944) and others. Multiple polyposis of the large bowel with supervening carcinoma is recognised as a familial disease and many examples are recorded by Lockhart-Mummery and Dukes (1939).

Neurofibromatosis with sarcomatous change often shows a familial association. In addition, there are reports of families in whom two or more members have been affected with leukaemia (Neel, 1953). Nevertheless, there are few references to the frequency of sarcomas in families. This is not surprising for mesenchymal tumours are rare. For this reason it is worthwhile to record two cases of sarcoma which have occurred in one family, a liposarcoma in one patient and a giant follicular lymphoma in a brother. Apart from this the family history is not remarkable; the father died of vascular disease at the age of 50 years, the mother is alive and well. The history of the previous generation is untraceable. There are four sons, two of whom are affected by tumour and constitute the basis of this report; the other two are well.

Case Reports

Case 1

A male aged 29 years noticed a small lump below the right groin since 1942. It began to enlarge slowly in 1945 and by 1953 was 4 inches in diameter. The tumour was removed locally at another hospital in April, 1953, and this was followed by deep X-ray therapy to the groin and right loin. In December, 1953, a small recurrence was noted at the lower end of the scar with some swelling of the right lower extremity and left sciatica. Physical examination was essentially negative except for the small lump in the scar and some thickening of the right pelvis felt per rectum. On 12th Jan., 1954, the recurrence of the thigh was excised. This was now found to extend around the femoral vessels, 8 inches down the thigh and upwards along the iliac vessels almost to the sacrum. These areas were cleared and the wound healed well.

On 22nd Jan., 1954, X-ray of chest showed a small mass in the anterior mediastinum; no abnormality was detected in the lungs. As this was considered possibly a new primary growth and there was no real evidence of growth elsewhere, and the patient had had full tolerance dosage of radiotherapy, it was decided to attempt to resect this tumour. He was also getting signs of obstruction to the thoracic inlet. On 8th Feb., 1954, anterior mediastinotomy was performed. A large soft diffuse growth was found occupying the whole of the anterior mediastinum and invading the sternum. Contiguous pleura and pericardium were invaded. As much as possible was removed to relieve the chest compression. The subsequent story was one of increasing interference with the venous circulation of the head and neck, dyspnoea and intractable sciatica. Cordotomy was attempted but abandoned due to venous bleeding. He died 1 year after his first surgical operation and 12 years from the first appearance of the tumour.

Pathological features

The tumour from the right groin was irregular in shape and measured 2 inches in diameter. It was pale, soft, and extremely friable, with areas of increased vascularity and haemorrhage scattered throughout. The neoplasm in the pelvis was partly yellow and fatty and partly pale and gelatinous. The biopsy sample of the tumour mass in the mediastinum was composed of soft gelatinous tissue.

The microscopical features were characteristic. The tumour showed a great variety of structure, ranging from mature adipose tissue to cellular areas of sarcomatous appearance with plentiful mitotic figures (Fig. 1). The latter kind of tissue constituted the bulk of the growth. The malignant lipoblasts varied in size and shape, sometimes reaching great proportions, and many were vacuolated. Frozen sections stained with sudan 111 showed abundant fat within the cells, more marked in some places than in others. Areas of myxosarcoma-like tissue were present and intermingled with the lipoblasts. There was also widespread oedema which resulted in pseudocystic degeneration, and in many parts the tumour was the seat of haemorrhage and necrosis.

The histological characters of the neoplasm in the mediastinum were very similar, but with many areas of densely fibrous tissue which appeared to be an integral part of the tumour.

Commentary

It is presumed that the tumour arose in the subcutaneous fat of the thigh. There were no pre-existing lipomas. However, in view of the wide involvement of the retroperitoneal

tis-ues, it is possible that the tumour was originally a retroperitoneal one and that it subsequently erupted under the inguinal ligament along the femoral vessels.

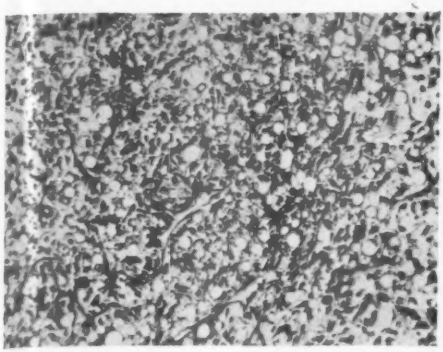

FIG. I. Liposarcoma showing malignant lipoblasts in various stages of differentiation. (x 137)

The two widely separate liposarcomas have appeared successively and it is of some interest to decide whether this case is an example of multiple independent tumours or of metastasis formation. Metastases do occur. They have been recorded by Stout (1944) in several of his cases and by other authors. On no particular evidence we felt that the mediastinal tumour was a second primary lesion and at death there seemed to be no tumours present except in the retroperitoneum and mediastinum, which were considered as extensions of incompletely removed primary tumours. Radiologically we were never able to demonstrate any secondaries in the lungs. Unfortunately a necropsy could not be obtained.

A valuable recent account of liposarcomas is that of Stout (1944) who records 41 cases and reviews 134 previously reported cases. All grades of malignancy are encountered. Our patient lived for 12 years from the first signs of disease. According to Stout (1944) some liposarcomas are radiosensitive. The present tumour was completely resistant to radiotherapy and to surgery.

Case 2

A man aged 38 years had noticed a lump in the abdomen 11 months previously. On examination a large hard fixed mass measuring 4 x 4 inches was palpable just below the umbilicus. At laparotomy an extensive retroperitoneal mass was found to extend from the sacrum to the diaphragm. No abnormality was detected in the viscera. A biopsy sample was taken of the tumour mass. Radiotherapy was instituted and the mass resolved completely within two months. On 16/4/51, 15 months after the first signs of tumour, the patient had an attack of intestinal obstruction due to a band. Laparotomy showed no obvious recurrence. Convalescence was uninterrupted. On 9/5/52 enlarged lymph nodes were evident in the left supraclavicular region but these resolved with radiotherapy. On 23/12/52 enlarged lymph nodes above the right clavicle and in the right axilla were found. These were irradiated and they subsided. On 15/2/54 further X-ray therapy was given to the right axilla. On 25/6/54 X-ray revealed a left pleural effusion and a mediastinal mass. Nitrogen mustard (0.7 mgm., 4 doses) was given but there was no response after two weeks. Further radiotherapy was instituted to relieve dyspnoea and chest inlet compression. Eight months later the patient remains well but with a probable residual growth in the chest.

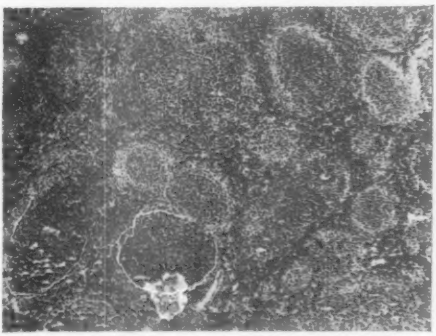

FIG. II. Giant follicular lymphoma. The lymph node shows abundant well-differentiated follicles. The clear spaces surrounding some of these follicles are a noteworthy feature of this condition. (x 31)

Pathological features

Microscopical examination of the abdominal mass showed the usual structure of a giant follicular lymphoma with many well-differentiated large lymphoid follicles closely packed together (Fig. 2). Characteristically, in silver impregnation sections, each follicular nodule was surrounded by a condensed meshwork of reticulin fibrils. Areas traversed by trabeculae of hyaline collagenous tissue were present. Mitotic figures were frequent.

Commentary

These lesions are to be regarded as well-differentiated forms of lymphosarcoma. First described by Brill, Baehr and Rosenthal (1925) who originally considered the condition to be a hyperplasia, it is now regarded by most workers, including Baehr and Rosenthal (1927), as a type of malignant lymphoma. A feature of this disease is its

rapid response to irradiation and our patient is still alive 5 years after the first appearance of the tumour.

DISCUSSION

Malignant tumours of adipose tissue are of rare occurrence. Thus Moreland and McNamara (1942) found nine liposarcomas in 16,000 tumours of different kinds. The presence of liposarcoma in one patient, and of lymphosarcoma in a brother is, therefore, unusual; and it is with two such cases that the present paper is concerned. Their familial occurrence is undoubtedly the result of chance.

It is not proposed to deal at length with the morphological features of these lesions. Such changes for liposarcoma have been discussed by many authors, including Geschickter (1934), and Stout (1944). However, certain points should be stressed. Particularly noteworthy is the great variation in histological structure of liposarcoma, which is a recognized feature of most of these tumours. This has often led to difficulties in diagnosis. In the first place, many of these tumours show an anaplastic cellular structure and, unless they are sufficiently differentiated, may escape recognition. Secondly, malignant tumours of other kinds may be diagnosed as liposarcomatous, merely because they have undergone fatty change. Therefore, it is clear that careful study is necessary in the histological diagnosis of liposarcoma.

The microscopical appearances of giant follicular lymphomas are too well known to require description. They are well illustrated in many papers including those of Symmers (1938, 1942), and Gall and Mallory (1942). Most distinctive, of course, is the follicular pattern. In their usually slow growth to large sizes and in their relatively favourable prognosis they differ from other forms of lymphosarcoma.

SUMMARY

Two cases of sarcoma, a liposarcoma and a lymphosarcoma, are described in one family. Such a familial occurrence is rare and purely fortuitous.

ACKNOWLEDGEMENTS

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THE PRESENT DILEMMA IN CANCER THERAPY

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"Yet every physician is prone to exaggerate the inveterate nature of the disease which he has cured.

—Edward Gibbon: *The Decline and Fall of the Roman Empire*, Chap. XXVII.

THE satisfactory treatment of any condition depends on the adequate knowledge and understanding of its characteristics. It is appropriate, therefore, that in any consideration of the present position with regard to the treatment of cancer, that we should consider the present-day views regarding its nature.

Many advances have been made in the last three decades in cancer research and a formidable volume of information has been collected. Some of this has a direct bearing on treatment and modifies, or should modify, some of the old established and deeply entrenched myths and shibboleths. At the same time it is also clear that, despite these very encouraging results, progress towards the elucidation of the fundamental nature of cancer has been negligible.

Pathology

One of the most important features, and one which is apparent to all who have made even a superficial study of the problem, is that we are not dealing here with one condition but rather with a conglomeration of "enigmas collectively known as cancer." Because they are commonly linked together observations made on one type or group are often applied to others which are, in fact, dissimilar. The resulting false deductions are usually completely misleading. Furthermore, this applies particularly with regard to treatment of the condition since what is adequate for one form may be completely inadequate for another and the large operation on or intensive treatment of one may be quite unnecessary in the other. The possible errors in the interpretation of results of treatment also are well known or can be readily appreciated.

For these reasons it is essential that the various types of neoplasms should be carefully segregated. When the differences between tumours, with regard to the invasion and destruction of adjacent tissues and their spread to involve other parts of the body, are considered it is apparent that there are greater differences between different types of tumours than there are between some of the tumours and certain non-neoplastic conditions.

Many of these differences are indicated and emphasized by terminology and any classification such as, for example, the histological method provides some measure of differentiation between the different types. At the same time different examples of one type of tumour, even in the same organ, may have different rates of growth and capacities for development of metastases. One of the most important principles is that benign conditions should be clearly differentiated from malignant ones and that results of treatment of one group should not be applied to the other.

Such observations are basic and have been appreciated for many decades. It is proposed here to consider some of the more recent work that has been carried out principally in the laboratory.

Aetiology and Pathogenesis

Until about three decades ago it was generally thought and stated that the "cause" of cancer was unknown but, since that time, a great deal of information has been collected and confirmed. Several agents — chemical, viral and physical — have been demonstrated to be "causes" of the condition; indeed we are faced, these days, with a multiplicity of causes. Moreover, in addition to the various factors which act on the tissues it is quite clear that there are peculiarities in the tissues themselves which determine the form of the tissue development that will take place in the particular circumstances. The various factors could be considered in a section on

aetiology and the tissue responses in one on pathogenesis but in all circumstances we find the two closely interrelated.

The accumulation of information has been rapid and, continually, hypotheses are being developed to explain the observations; but advance has been so rapid that these are periodically and frequently outmoded. Each of the aetiological agents demands and deserves extensive consideration in its own right but here it is only possible to give them a passing mention.

Although the carcinogenic characters of soot were remarked upon by Percival Pott and experiments were carried out with tars early in the present century, it was not until just over twenty years ago that the cyclic hydrocarbons in purified form were obtained. The benzanthracenes, benzpyrenes, methycholanthrene, benzcarbazole, amongst many others, have been investigated not only from the point of view of their biological effects but also of their chemical and physical characters.

There is, in a condensed polycyclic molecule, a part known as the K region where there is a concentration of π electrons. It is this region of the molecule which possesses the carcinogenic properties. Different hypotheses have been propounded to explain this phenomenon of which the two most important are those of electronic resonance and molecular orbitals. The important point is that here we have a well-developed relation of complex biological phenomena to the principles of quantum physics.

As a result of the determination of electronic configurations of the molecules it has been possible to predict the characteristics of compounds which had not previously been used nor even, at that time, synthetized. The demonstration of the importance of this feature regarding one group of substances seemed certain until some compounds were produced in which this did not apply.

This discrepancy has stimulated a great deal of interest and the explanation may be that there is more than one mode of action but also, as has been suggested by some of the investigations, that the K region may be only important at one stage in a complicated process.

The action of an alkylating agent (mustards — epoxides) inducing cross linkage of fibrillar proteins (radiometic action) is an example of an alternative process.

A significant feature of the phenomenon of chemical carcinogenesis is the latent period, sometimes quite long, between the time of application of the chemical and the development of the tumour. The latent stage has attracted great interest and the possible relation to the pre-cancerous states of clinical surgery has been studied. It has generally been recognized that the development of tumour characters is not a single process but can be divided into an initiating and a promoting stage and that the fundamental change in the cell is probably a matter of several "mutations."

The complicated nature of the phenomena is indicated by the demonstration, in some circumstances, of co-carcinogens and also of anti-carcinogens. These last are quite often substances which in themselves would be carcinogenic but may be normal substances, for example, protection from azo-dye carcinogenesis by riboflavine. That it is a matter of competition for various components of the cells by the antagonistic substances in some cases and interference with the process normally resulting in tumour development in others has, in some examples, been demonstrated but in many the mode of action is still obscure.

It seems certain that the chemical carcinogen combines with a component of the cell; details of this phenomenon are still being elucidated. Thus, though much of the theoretical side of the phenomenon may still be in the field of speculative mathematics the general importance of what is a group of extremely complex physico-chemical phenomena seems clear.

Virus

In general it can be said that cancer workers are divided into two groups. Those that accept the viral origin of most tumours and those who do not agree. There has been a considerable amount of thalamic activity over what is regarded by some to be a "false antithesis." There can be no doubt that some tumours are due to the presence of virus but the "interest in virus induced tumours does

not lie in the naive assumption that all tumours are the result of a virus infection."

It is important that the number of tumours demonstrated to be due to virus infection is quite small. There are the leukaemic conditions in birds (if one accepts the leukaemias as tumours), the Rous sarcoma in the chick, the Shope papilloma of the rabbit, the adenoma of the kidney of the frog and a few warts in the higher animals including man. The Bittner milk factor in mice is regarded as being related but its significance is not at all clear.

An important point is the definition of a virus. The proponents of the viral hypothesis include cell components, which appear to play an important part in the development of a tumour, in the definition of a virus whereas the antagonists of the view do not. It seems probable that in another twenty to thirty years the current idea of what is a virus (and therefore its relation to cancer development) will be very different from what it is today.

Physical factors

These are of quite diverse characters and emphasize the multiplicity of factors which may give rise to tumour. However, though heat, ultra-violet light waves or short waves (of radiation) all give rise to tumours, simple trauma even though repeated does not have this effect. This is discussed again.

Nutritional factors

The nutrition of an individual does not have a clear-cut relation to tumour development probably because a large number of interrelated factors is in action. In some cases over-nutrition has been shown statistically to be related to the development of tumours and, in other circumstances, poor nutrition. Probably the difficulty here lies in what has been an attempt to over-simplify a complicated matter, that is to say, nutritional disturbances may give rise to a complicated series of changes in the tissues which, at various different levels, may produce the changes which ultimately give rise to a neoplasm.

Hormonal influences

The close similarity chemically of some of the hormones with the well-known carcinogens has stimulated and kept alive an active interest in the relation of the hormones to tumour development. Furthermore tumours frequently develop in organs which are the site of hormonal stimulation, for example, the breast and prostate. Careful analysis of the changes, however, would seem to indicate that the association is an indirect one but a great deal of work is being done in this field. One important result of the work is that hormones have been demonstrated to influence the growth of tumours (of the appropriate cell type) in a way that indicates that the old idea that tumours are autonomous is fallacious.

Recent improvements in the ability to separate the various fractions of protein from each other in the serum by, for example, electrophoresis have shown not only that there are changes in the proteins when tumours develop but also that the chemical agents unite with specific fractions. This has been shown not only with the polycyclic hydrocarbons but also with the diazo dyes. This has opened up a wide field which is being actively explored at the moment.

A great deal has been made of the differences in the protein fractions but most of these appear to have been over-emphasized and it is probable that changes in the proteins which are in the smallest quantity are the most significant.

Trauma and tumour development

This question is mentioned specifically because it is one which frequently attracts the attention of the practising surgeon and also is one on which he is sometimes asked to give an opinion.

In the first place it is clear from what has been said that the phenomena in the development of a tumour are extraordinarily complex and are related to complicated physico-chemical phenomena which, with the recent amazing advances in physics, are beginning to be understood even if the light thrown on them is still yet but a glimmer.

At the same time some direct experimental work has been done. For example, it has been shown that in some of the animals repeated small injuries or chemical irritation to an area where a carcinogen has been applied will result in the more rapid development of a tumour. Nevertheless a tumour does not develop however long irritation is applied in the absence of a carcinogen.

Another important point, which is applicable to all aspects of cancer research, is that this observation only applies with certain material and in certain species of animals. The observation made in one animal cannot be applied directly to another species. Furthermore observations of this kind are few and far between and in most circumstances and with many of the carcinogens irritation, particularly of a mechanical kind, does not facilitate nor expedite the development of the tumour; indeed in many cases it inhibits it.

When these observations are taken into consideration together with the latent period which indicates that whatever the exciting factor is, it is probably a long-acting one, the significance of trauma diminishes in importance. The complexity of the problem is indicated by the observation that in the epidermis the cells on which a carcinogen acts have been desquamated and replaced long before the latent period for the development of the tumour has passed so that the cells which become cancerous are not those on which the agent actually acted.

These various aspects of the problem are presented here to indicate that a person, who has not had special training and experience in modern cancer research but who gives an opinion with regard to the relation of trauma and cancer, is rather like the child with a toy aeroplane who gravely voices his opinions on the aerodynamics of a jet aircraft.

TREATMENT

One of the greatest advances in modern times has been the integration of the various forms of treatment of tumours. Each department has in itself made great strides but no one has very significantly increased the number of cures.

As more and more cases are being intensively investigated and treated and as the methods of diagnosis have been modified more "early" cases have been included. Many of these require much further and more intensive study because it seems probable that some of them, such as the cancer "in situ" and some of the pre-cancerous states, have been wrongly assessed.

On the other hand the general condition of the patients has tremendously improved. Even though the patient may die ten or fifteen years later from the disease that he should have been alleviated of the very distressing symptoms for that time is complete vindication of a method of treatment and is in the true Hippocratic tradition.

Surgery

It should be said at the outset that surgery is not the complete answer to the question of cancer treatment; it is one of a number of partial answers. The aim of surgery is the eradication of the disease and its success depends upon the tumour's localization and accessibility. If a growth be truly malignant it is not really localized and usually has become bloodborne early. This means that in many cases complete removal of the condition is not practicable.

This does not mean that the local lesion should not be removed. Indeed, if the removal of a superficial lesion will prevent fungation, ulceration and perhaps obstruction to a tube, then its removal is clearly indicated. At the same time any extensive operation should be planned for a specific reason and an unnecessary major procedure should not be carried out without the most precise indications; it must always be remembered that injury to the body (and of course any operation must be this in some measure) often stimulates and accelerates the growth of distant metastases. The inhibition of the tumours by others of the same kind in the body is a phenomenon that has been the subject of considerable experimental research but, apart from this work, the rapid growth of metastases after the removal of a primary tumour has become, in recent years, a well-known clinical phenomenon.

Assessment of the patient as well as the tumour is of first importance. In the first place is an operation justified? This would depend on the age of the patient and the type of the disease. For the reasons just mentioned above it may be better to treat an osteogenic sarcoma by deep therapy rather than by operation, for a period, and recent modifications of management in the case of carcinoma of the breast are well known.

Are the large operations justified? There seems to be no doubt in many cases of carcinoma of the uterus and cervix. When the operation involves loss of a limb or the production of an intestinal fistula (colostomy) a

great deal depends on the length of time that the patient is expected to live after the operation. Where, as happens in many cases, it is clear that the patient cannot live for many months a disability for which he will not have time to accommodate merely adds to his troubles and does not alleviate the overall condition. The treatment of the disease in these circumstances without reference to the psychological problems of the patient as a whole, is, in my view, one of the most serious defects of the modern, otherwise wonderful, age of mechanical surgery. The problem of a high operative mortality raises other and different questions of morality and ethics. It is generally recognized that adequate "follow-up" of patients treated for malignant disease is essential to a satisfactory understanding of the limitations of any method of treatment. Such investigations are time-consuming, expensive and sometimes difficult and thus information is being collected only slowly. It is not yet adequately appreciated that present-day views of the value of various treatments embody a great deal of unjustified optimism.

Radiotherapy

The principles which should govern the application of radiotherapy to cancers are similar to those in surgery. There is the advantage that gross destruction of tissue does not occur so that radiotherapy is applicable in cases where surgery might not be reasonably considered. On the other hand there is no certainty that irradiation will kill all the cells in the area in the way comparable with that by which a surgical operation will remove them. Nevertheless this disadvantage is outweighed by the practicability of attack on topographically inoperable conditions.

The disability of radiation sickness, however, is the counterpart of the complications mentioned above. It is of no real value to the patient if he is to spend a considerable part of his remaining weeks or months of life in a state of misery from the results of the treatment when the prospects of actual cure are remote or non-existent.

Radio-isotopes

Isotopes of various elements have been used as a means of more precise irradiation of certain parts of the body without damage to superficial areas.

I^{131} has been used in carcinoma of the thyroid gland. The principle underlying its use is that since the thyroid cells produce thyroxin they will employ the radio-active iodine which will then be concentrated in the thyroid gland and will act on the tumour. The fallacy of this argument is that only differentiated cells which are secreting thyroxin will take up the radio-active iodine. The method is therefore useful in differentiated tumours but in the non-differentiated tumours it is useless. In this regard it is possible that a combination of this method with radiotherapy, where the rays affect the less differentiated cells to a much greater extent, might be advantageous but it is unlikely that even a combination of these methods will give complete cure.

Radio-colloidal gold (Au^{198}) has been used particularly for the treatment of lymph node metastases in carcinoma of the uterus. The principle is that the material in suspension is injected into the broad ligaments and then is carried by the lymphatics to the lymph nodes. The fallacy is that the lymph nodes containing metastases will have blocked lymphatics, either because of the cancer cells filling them or because of the associated fibrosis, and any colloidal gold will be carried to unaffected lymph nodes. Therefore, the method must be ineffective.

One very satisfactory form of treatment is the use of an isotope of sodium (Na^{24}) in the treatment of papilloma of the bladder. A suspension of the isotope is run into the bladder and acts immediately on the superficially placed papillomata. This has been remarkably successful. The disadvantage is that the radio-active sodium has a very short half-life of only a few hours and therefore the material is only available in an effective form at a place close to an atomic pile, a cyclotron or similar apparatus. Incidentally, this method of treatment would be quite ineffective with an actual carcinoma of the bladder.

Hormones

It is necessary only to contemplate the remarkable changes that occur in various tissues of the body as the result of the action of various hormones to appreciate their potency. Proliferations and, in other circumstances, rapid atrophy of tissue is seen to

occur — most characteristically in the accessory sex organs. Similar changes occur in tumours composed of these types of tissues. An example of naturally occurring activation of a tumour by hormones is to be seen in some of the cases of carcinoma of the breast which has been small and inactive for many months (sometimes a year or two) and becomes a rapidly growing and fatal growth in the early stages of pregnancy.

As mentioned earlier the effect of the hormones on some of the tumours clearly indicates that these growths are indeed part of the body and are affected by those influences which control the ordinary cells.

This is a wonderful weapon if wisely used and though it is applicable, as yet, to only a few tumours the improvement in the state of the patient as well as the control of the tumour is one of the more cogent reasons for including it in our armamentarium.

Chemical agents

The most important group of chemical substances which influence "tumours" are sulphur mustard, nitrogen mustard and related substances. These have an action principally on the haematopoietic system and thus on the conditions where there is an increase of these tissues. Even if the particular diseases, such as the leukaemias and Hodgkin's disease, are accepted as neoplasms (and not all would agree with this) it is apparent that these substances are significant in only a small range of conditions. Since they affect the normal cells as well as the abnormal ones, they have a distinctly limited value and thus come into line with the other therapeutic agents mentioned.

A wide range of other substances has been investigated and, as suggested earlier, these include compounds which may themselves be carcinogenic. The number of substances investigated is large and the groups cover a very wide field. With a continued study of this aspect of the problem it is quite likely that valuable agents will be found. At present most of the work is being done on laboratory animals and therefore any results obtained need not necessarily be directly applicable to man. An example of this chemical inhibition in man is the effect of Vitamin B_{12} in significantly increasing the frequency of spontaneous regression of neuroblastoma in children. The basic study of the mode of action of these substances, already demonstrated in some cases as being on specific enzyme systems in the cells, is extending our knowledge in a direcion which should, before long, be fruitful from the point of view of therapy.

Treatment of complications

This aspect of the general problem is of the greatest importance. When considering the pathological features of neoplasms in relation to symptoms it soon becomes clear that nearly always the symptoms are due to complications of the primary tumour such as obstruction of tubes and secondary infections with ulceration and haemorrhage, and that many of the outstanding features of the tumours therefore such as anaemia and cachexia are in fact due to these complications.

These may be dealt with by the removal of the primary condition surgically and of course may be alleviated by the diminution in activity of the growth following radiotherapy; in addition the recent development and application of appropriate antibiotics has become one of the outstanding methods of alleviating the symptoms of the cancer patient.

As mentioned earlier this is the effective aim of modern therapy, surgical or non-surgical, and constitutes the twentieth century contribution to the management of this disease.

If emphasis is placed on this aspect of the treatment of cancer rather than on vain attempts to cure what is, from the very nature of the disease, incurable, the contribution of modern medicine is seen in its appropriate perspective and, incidentally, the patient has more reason for gratitude than if he should be subjected to heroic but ineffectual procedures.

SUMMARY

Neoplasms (of which cancer is one of the most numerous and important examples) comprise a large number of different forms of growth. They are similar in that they are complex variants of the normal cells and thus the factors determining their mode of growth are those which are inherent in the growth of the normal cells, that is to say, they are

inherent in life itself. For this reason it is probable that the answer to the cancer question will be bound up in the answer to the fundamental problems of biology.

In any case it is not a matter of a single or simple problem to which there is a single or simple answer.

Each group differs from the others and in each group there is a considerabe variety of appearance and activity which are the indexes of differences of rates of growths and methods of spread, amongst other features. It is therefore necessary to take each case on its merits; none can be dealt with adequately by any rule of thumb method and, most important of all, none can be assessed on the basis of other less malignant conditions.

It is particularly important that the non-neoplastic states which resemble tumours and the least malignant of the neoplasms should not be given undue prominence. The understandable human characteristic remarked upon by Gibbon in his day is still with us but, with the amazing improvements in our knowledge and our armamentarium, we can surely face the issue squarely and appreciate that, though we have travelled a considerable way along the road, we are still a long way from our destination — an understanding of either of those enigmas — cancer or life. Tumours are one manifestation of the phenomena to be observed in the living cell and, from many points of view, our problems become clearer, if apparently more formidable, when we appreciate that the one is bound up in the other and that any explanation of cancer development which does not embody an interpretation of fundamental biological processes, will be incomplete and futile. The road ahead is long and arduous and, correspondingly, treatment will advance only gradually and tardily. It is neither wishful thinking nor unfounded claims of successful therapy, but the unearthing of information regarding the nature of cancer (and, as just said, of life itself) that will determine future progress.

SYNOVIAL CYSTS IN BONE

By J. Douglas Hicks

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THERE is nothing so intriguing as a cyst in bone. From the moment the shadow on the wet film is inspected by the radiologist an atmosphere of tense speculation develops and is carried to the orthopaedic clinic. One can picture the discussion aroused and the train of investigations which may follow. In the clinical history and examination, in the X-ray film, and in biochemical analyses there may be clues but the suspense excited by the radiolucent area is often carried to the operating theatre and even to the pathologist's microscope.

Nearly all bone cysts are not cysts in the true sense of the word, for the definition of a cyst is an abnormal cavity containing fluid. Generally a cyst is considered to have a definite wall or lining which is different from the normal tissue of that part.

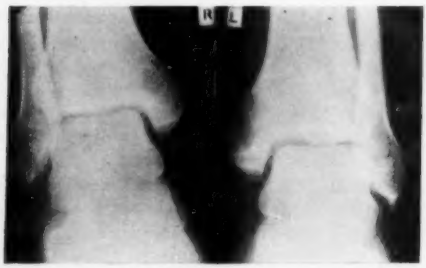

FIG. I. Case 1: A well-defined radiolucent area 2.5 cm. in length is to be seen in the left medial malleolus, a similar smaller area in the right medial malleolus.

The term "bone cyst" is used radiologically and surgically to denote a circumscribed radiolucent area in bone, an area which does not contain the normal solid bony structure. Naturally, the contents of this area may vary from non-calcified bone trabeculae of normal arrangement through fibrous tissue to a fluid material, from localized rarefactions of bone to replacement of bone by cellular tumours, primary or metastatic.

A line may be drawn, perhaps, between those cavities which contain fluid merely as a result of some secondary change such as degeneration or haemorrhage and those which have a distinct lining, different from bone, and contain fluid as a consequence of the nature of the lining. The term "bone cyst" should be reserved for the latter type. A hydatid cyst of bone is an example of a true bone cyst.

Cysts of bone containing synovial fluid are not uncommon in osteoarthritis. Small cavities connected with the joint by a crack in the damaged cartilage are formed in the bone adjacent to the joint. Such osteoarthritic cysts have been described by Landells (1953). The cysts described here are of a different type and are not necessarily near a joint and apparently have no communication with a joint.

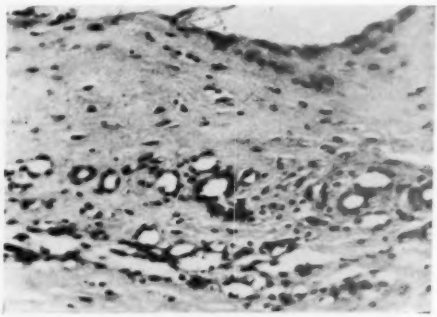

FIG. II. Case 1: Photomicrograph of lining of cyst from left medial malleolus. Connective tissue cells form the wall and also the surface lining of the cyst. Numerous small vessels in the outer portion of the wall are typical of synovium. (x 290)

Case 1

The first example is from a man of thirty years who complained of a vague but persistent pain in the region of the medial malleolus of the left ankle. In the X-ray film of the ankles (Fig. I) a well-defined radiolucent area about 2.5 cm. in length was seen in the left medial malleolus. A smaller area, symptomless, was present in the other medial malleolus. An operation was advised and the bone explored. A cyst lined by relatively smooth membrane and containing mucoid fluid was removed. The section shows the connective tissue lining of the cyst to have

a clearly defined surface (Fig. II). Small coagula of fibrin are present in the cavity or adherent to the surface of the lining or to one or two fringes projecting from the surface. In some parts the connective tissue is dense and the cell nuclei larger than in ordinary fibrous tissue, the general structure resembling that of synovial tissue. There are scattered cells in the loose coagulum in the cavity, there are many small arterioles at the edge of connective tissue lining, appearances confirming the resemblance to synovium.

The cavity in the malleolus of the left tibia was treated by filling it with bone chips. At the present time, four years after operation, the patient has no complaints, the small cyst in the right medial malleolus is still present.

FIG. III. Case 2: The cyst in the upper end of the right tibia with sharply defined upper and anterior margins measures about 6 x 3 x 2.5 cm. in size.

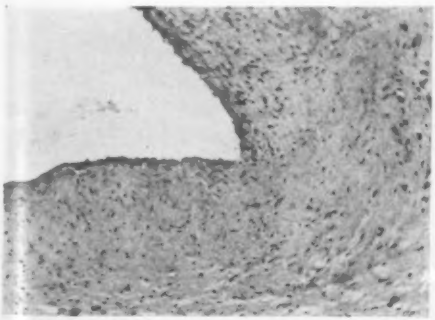

FIG. IV. Case 2: Photomicrograph of the thick fibrous wall lining the cyst of the tibia. The cell nuclei are small, the surface is of flattened cells. Mucoid droplets, seen as clear spots, are fairly numerous towards the surface. (x 140)

FIG. V. Case 2: Photomicrograph of lining of cyst of tibia at higher magnification showing details of surface cells which are partly lifted off during preparation of the section. The mucoid droplets are scattered profusely amongst the connective tissue fibres. (x 290)

Case 2

A second example is from a young woman of twenty years who had pain in the right lower leg for four months after she had fallen over and hurt her leg. A cyst was seen in the upper end of the tibia in a routine X-ray film (Fig. III). The tibia on the left side was normal. The cyst was curetted and filled with bone chips from the iliac crest. It was found to be lined by a fleshy membrane, yellowish in colour and to contain clear pale yellow fluid. The approximate dimensions of the cyst were 6 x 3 x 2.5 cm. The sections of the wall of this cyst are similar in appearance to those of the wall of the first example. There is a connective tissue band 2-5 mm. thick with a smooth surface which in some parts appears to be synovial (Fig. IV). Many tiny vacuoles are present amongst the connective tissue cells so that in some places the lining membrane has a mucoid appearance (Fig. V). As well as some recent haemorrhage, probably due to surgical trauma to the large endothelial-lined channels in the outer part of the wall, there are crystals of iron-containing pigment. A light sprinkling of lymphocytes is present at one or two points in the loose areolar and fatty tissue outside the main wall of the cyst. Trabeculae of bone are arranged normally but osteoblasts are more prominent than usual. Superficial to the bone there are several somewhat irregular but generally linear strands of haematoxylin-stained material, surrounded by layers of connective tissue. These appear to be the remnants of bone trabeculae, the osteoid tissue having been replaced but the calcified portion of the matrix is left behind. In the two years since operation there has been continued good progress.

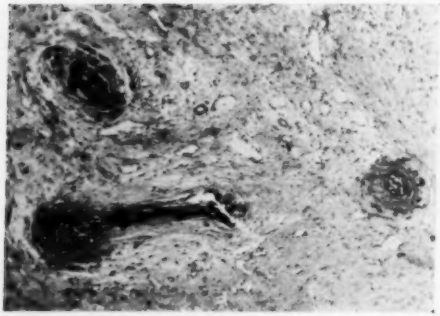

FIG. VI. Case 2: Photomicrograph of wall of cyst of tibia showing the remains of three partly absorbed trabeculae, seen as irregularly oval or linear calcified areas bounded by layers of delicate connective tissue. (x 90)

with a rather thick somewhat papillary wall and containing yellowish slightly turbid fluid. The cyst was lined by thick folded synovial membrane, infiltrated heavily with masses of lymphocytes to form the picture characteristic of chronic villo-nodular synovitis (Figs. IX and X). Higher magnification shows a prominent epithelium-like layer of synovial cells on the surface with more typical flattened synovium in some areas (Fig. XI). Beyond the synovial and lymphoid tissue there are strands of fibrous and areolar tissue which form the outer wall of the cavity. Other areas show in further detail the synovial folds and fringes with greater or less accumulation of lymphocytes and lymph follicles. In this case the cyst in the ulna is lined not only by recognizable synovial tissue but by chronically inflamed synovium.

In further X-ray films taken some months later the left olecranon process was filled in, there was no change in the cystic areas on the right side. More recent films, two and a half years after operation show that the cyst on the right side has disappeared spontaneously.

FIG. VII. Case 3: Left elbow. The olecranon is almost replaced by a lobulated cystic area which extends up into the coronoid process.

FIG. VIII. Case 3: Right elbow. There are smaller, less obvious radiolucent areas in the olecranon, near the joint surface.

Case 3

A third example of cyst lined by synovial membrane was found in a man of sixty-five years who in 1948 complained of pains in the right shoulder and later in the left shoulder as well as in the right hand. Three years later, in 1951, he complained of various aches and pains, most recently in the elbow joints in which a creaking crepitus was detected. In X-ray films of the elbows a large radiolucent area occupied most of the olecranon process of the left ulna (Fig. VII). Smaller cavities were present in a similar situation on the right side (Fig. VIII). It was thought that the rarefied area on the left side approached the joint surface so closely that fracture might occur and it was decided to operate and fill in the cavity with bone chips. A true cyst was found

Case 4

It is possible that a fourth example is to be seen in the small cavity in the talus in another case, a man in his twenties. A radiolucent area about one centimetre in diameter is present in the middle of the neck of the astragalus, well away from the ankle joint (Fig. XII). As the cyst gradually enlarged, it was opened and curetted. The cyst contained clear fluid and was lined by a smooth membrane which was not examined microscopically. In the three years since operation the cyst has persisted and has definitely enlarged.

FIG. IX. Case 3: Photomicrograph of the wall of the olecranon cyst showing a well-defined psuedo-epithelial synovial surface with a papillary frond. Lymph follicles beneath the surace lie amongst strands of fibrous and areolar tissue. (x 50)

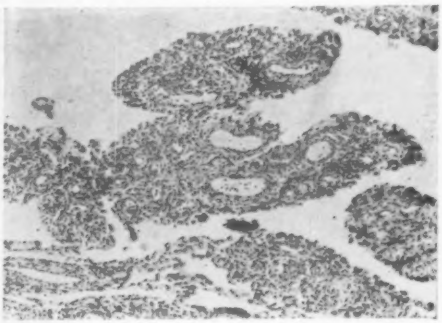

FIG. X. Case 3: Photomicrograph showing loose branching villi, with large vessels and small groups of lymphocytes, which line the cyst of the olecranon. The surface layer consists of large loosely-arranged synovial cells, some of which are desquamating into the cavity. (x 90)

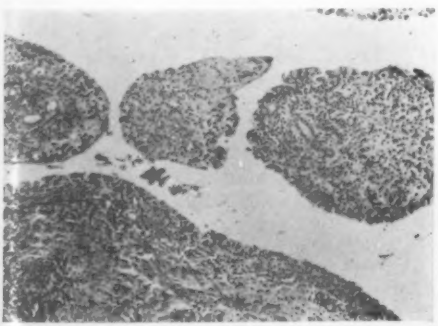

FIG. XI. Case 3: Photomicrograph of lining of cyst of olecranon, the villi containing numerous lymphocytes. A few of the larger synovial cells near the surface of the cyst are multinucleated. (x 90)

FIG. XII. Case 4: In the middle of the astragalus, in the region of the neck, is an oval radiolucent area about 1 cm. in longest diameter.

The significance of these cysts may be considered from a number of points of view.—

1. The nature of the lining membrane has been demonstrated as synovial in type so that these cysts may be termed "synovial."

   Bone and synovium are but special modifications of the skeleton and it may be anticipated that bone, cartilage, synovium, ligaments or tendons and possibly even muscle may differentiate from the basic tissue elements in a locus of the skeleton, provided the appropriate conditions are present.

2. What relation do these cysts bear to previously described cysts in bone? Possibly the nearest type is the solitary unicameral bone cyst, such as is described by Garceau and Gregory (1954). These unicameral bone cysts are usually found in young people and have a cavity incompletely filled with fluid and with a variable amount of connective tissue lining the wall. The unicameral cyst occurs mainly in the proximal ends of the femur and humerus but may be located at either

end of the tibia or in the calcaneus. Some cysts have resolved spontaneously but most have been treated successfully by curettage and filling with bone.

3. What is the manner of formation of the cysts?

Many suggestions have been put forward in attempts to explain the development of solitary bone cysts. If trauma played a significant part one would expect to find evidence of considerable haemorrhage and even in cysts of long-standing a good deal of old blood pigment might be found in the wall or the lining of the cyst. In Case 2 a small amount of old blood pigment was present in the wall of the cyst, and there had been an injury to the leg four months previously. The injury was relatively mild and the pain was in the lower part of the leg rather than below the knee. If trauma had caused such a large cyst one would have expected more signs of haemorrhage. Probably the injury caused some haemorrhage into the delicate tissues of the already present cyst. Inflammatory changes sufficient to produce resorption of bone trabeculae are generally associated with the formation of a definite abscess. In such cases the cavity is probably surrounded by dense bone and the lining of the cyst would consist of dense fibrous granulation tissue, a Brodie's abscess.

Apart from the factors of trauma and inflammation we have little knowledge of any other pathological processes which might determine a local resorption of bone with the formation of a simple cyst.

4. Does the conception of these cysts as "synovial" enhance our understanding of their nature? In the preceding paragraph no satisfactory explanation was offered for their formation, but if we regard the cysts as essentially an area of synovial tissue then they may be considered as a local transformation or metaplasia of tissue. We can conceive the possibility of bone becoming synovial tisue just as columnar epithelium can become multi-layered and squamous in type.

The actual stimulus which initiates the change may not be obvious. In two of the examples described the cysts were bilateral and although in each case only one cyst was opened, it is reasonable to suppose that the other cysts were similar in nature and that the determining factors were located in the areas of bone involved.

The possibility of reversal of the process and a return to bone can be readily entertained, and in Case 3 this is probably what has happened in the right olecranon process. It can be appreciated that the metaplastic synovial tissue would be liable to undergo those disease processes which may occur in synovium elsewhere in the body and the gross pathological change in the lining of the cyst of the left olecranon in the third case is not out of keeping with what might be expected in the synovium of the neighbouring elbow joint.

Fracture of the bone through the cyst would be dependent upon the degree of weakening of the bone by the cyst and on the application of the appropriate distorting force. Fracture is a definite risk in unicameral bone cysts, for it occurred in 65 per cent. of the 114 cases collected by Garceau and Gregory. There is no evidence that the metaplastic synovial tissue ever becomes neoplastic, although synovial tumours may develop in bone (Hicks, 1954). Indeed, the frequency with which the larger portion of a synovial tumour involves bony tissue (Wright, 1952) suggests to me that many synovial sarcomata which are said to have invaded bone actually arose in bone and spread outwards.

SUMMARY

Three simple cysts of bone lined by a connective tissue membrane have been described. They have been compared with solitary unicameral cysts of bone. The mode of formation has been discussed and reasons have been put forward for the classification of these cysts as "synovial."

ACKNOWLEDGEMENT

I am indebted to those surgeons, particularly Mr. B. T. Keon-Cohen, who have sent me the cysts and the case notes of the patients concerned. To Mr. R. Inglis I express my appreciation of the skill with which he has reproduced the X-ray shadows.

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THE MANAGEMENT OF ENDOMETRIOSIS OF THE LARGE INTESTINE

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THERE are innocent lesions of the large bowel which in some patients satisfy practically all the clinical criteria of malignancy. One such lesion is endometriosis, but carcinoma of the large bowel is so common and of such grave prognosis that one hesitates to consider this unusual diagnosis in a patient even when some of the presenting features perhaps do suggest it. It follows that these few unusual features are apt to be set aside. However, endometriosis of the bowel is not rare and errors in diagnosis and subsequent treatment are frequent leading to extensive, but not always necessary surgery. The problem will be illustrated by five case histories and an attempt will be made to point out features which may help to avoid future diagnostic errors.

Incidence

In 1930 Keene and Kimbrough reported 4 cases of obstruction of rectum and sigmoid colon in 118 cases of endometriosis. Three of these patients had had radical resections of bowel for suspected carcinoma. Masson (1935) drew attention to the frequency of intestinal involvement by endometriosis when he reviewed 576 patients operated upon at the Mayo Clinic between 1923 and 1934. The recto-vaginal septum was involved in 20 cases, the sigmoid colon in 14, the ileum in 2 and the appendix in 1 more. In 1948, from the same clinic, McGuff, Dockerty, Waugh and Randall reported 16 cases of the bowel causing intestinal obstruction. Cattell (1937) found bowel lesions in 17 of 104 patients with endometriosis treated at the Lahey Clinic. He divided the cases into three groups:

(a) those with endometriosis of the recto-vaginal septum;

(b) cases with endometriosis of the serous and muscular coats of the bowel due to extension of generalized disease from adjacent ovaries, Fallopian tubes or uterus;

(c) those with endometriosis involving the entire bowel wall producing discrete tumours. Lesions in this group often occurred in patients in whom the pelvic organs were free of disease and so were frequently mistaken for carcinomata.

An even greater incidence of bowel involvement was reported by Jenkinson and Brown (1943). Of 117 women seen, 47 had lesions of the rectum, sigmoid colon or recto-vaginal septum which did or could encroach on the lumen of the bowel causing obstruction. Intestinal obstruction actually was produced in 21 of the 47 patients.

Pathology

Lesions in patients with extensive pelvic endometriosis are not likely to be mistaken for carcinomata. At laparotomy there may be tarry cysts of the ovaries adherent to surrounding structures. The uterus may be enlarged diffusely due to adenomyosis or eccentrically due to fibromyomata. Scattered over the pelvic peritoneum, particularly in the pouch of Douglas may be early lesions of endometriosis, small bluish or black cysts, but more often adhesions around these lesions will have obliterated the pouch as the rectum is drawn up towards the cervix and the ovaries and Fallopian tubes are drawn down to become adherent to the base of the broad ligament (Macleod, 1946). The bowel may be involved by direct extension from any of these lesions to which it might have become adherent.

In most cases the cause of obstruction is an obturation of the lumen of the bowel by an extramucosal mass and in opened, resected specimens intact mucosa can be demonstrated throughout the length of the lesion resembling chronic diverticulitis rather than carcinoma (Fig. 1). A characteristic feature of endometriosis of the bowel is the rarity of mucosal ulceration although the mucosa may be con-

gested and adherent when the endometrial islands are found in the submucosa. Bleeding from the rectum is uncommon in this disease. Rectovaginal septal lesions are similar. They form hard, tender, extramucosal tumours in the anterior wall of the rectum and frequently invade the vagina producing bluish cysts or polypoidal masses of endometrium in the posterior fornix.

FIG. I. Photograph of a section of the lesion found in Case 2 showing unbroken colonic mucosa extending right through a localized mass of endometriosis involving the outer coats of the bowel.

The lesions in the bowel wall usually have a mottled dark red appearance on section due to haemorrhage into endometrial glands and minute drops of dark red fluid may be scraped from the surface (McGuff *et alii*, 1948). Where haemorrhage has been minimal or absent there are intersecting strands of fibromuscular tissue which stand out from a yellowish background, contrasting with the grey homogeneous granularity of a section of carcinoma. Histologically there are small islands of typical endometrium scattered throughout the thickened bowel wall. Small glands and tubules lined by columnar epithelium surrounded by a dense cellular stroma are found within masses of fibromuscular tissue (Figs. II and III).

When the bowel lesion is quite discrete and independent of pelvic endometriosis it is most likely to be mistaken for carcinoma. It may present as a hard constricting tumour with a puckered surface to which adjacent appendices epiplocae may have become adherent and incorporated. Occasionally there may be small bluish or black spots on the surface of the mass which may be the only features to arouse the suspicion that the lesion may not be a carcinoma.

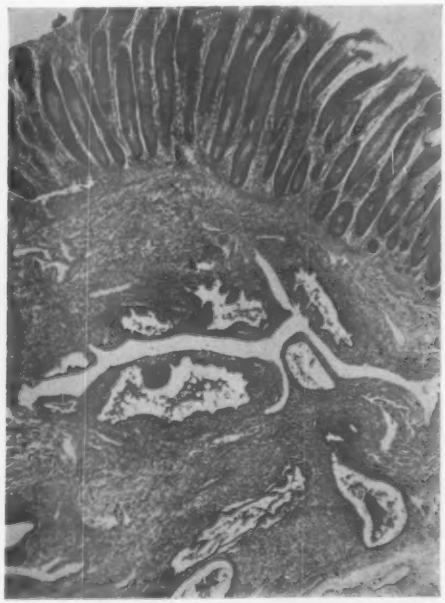

FIG. II. Photomicrograph of a section of endometriosis of the colon from Case 3 showing masses of endometrial glands and stroma embedded in fibromuscular tissue extending up to, but not into the colonic mucosa. (x 30)

Diagnosis

The diagnosis of intestinal endometriosis is strongly suggested if the bowel symptoms have a definite menstrual periodicity. Obstructive symptoms were much worse during the menses in 13 of the 16 cases reported by McGuff *et alii* (1948). Only 3 of their patients presented with gross rectal bleeding and then only at the time of the menses. In the absence of menstrual periodicity of symptoms the diagnosis of endometriosis is suggested by the following combination of circumstances:

(a) if the patient has not yet reached the menopause;

(b) if the bowel symptoms are long standing and accompanied by little or no rectal bleeding and no loss of weight. The average duration of the histories of Jenkinson and Brown's (1943) cases was 3.3 years;

(c) if there is a long history of acquired dysmenorrhoea, menstrual irregularity, menorrhagia, dyspareunia and sterility;

(d) if the patient has an enlarged uterus and/or ovarian cysts.

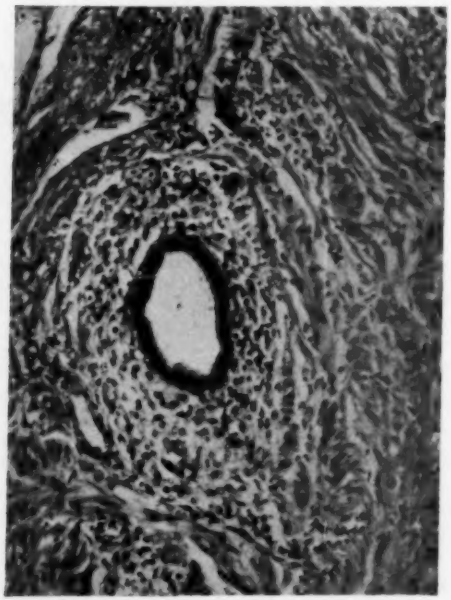

FIG. III. Photomicrograph of a section of endometriosis of the colon from Case 3 showing a small gland space lined by columnar epithelium and surrounded by a very cellular stroma. (x 180)

Because mucosal ulceration in endometriosis is unusual sigmoidoscopic examination is not very helpful and pre-operative biopsy will not be positive unless some ectopic endometrium lies in the mucosa or immediately beneath it. The appearance is not unlike that of diverticulitis; congested mucosa is seen at the mouth of a stricture.

Radiological examination similarly is not diagnostic, but endometriosis is suggested when a long, sharply demarcated filling defect is seen with apparently intact mucous membrane throughout its length, particularly when palpation shows the lesion to be fixed and tender (Cattell, 1937; Jenkinson and Brown, 1943; McGuff *et alii*, 1948).

Treatment

Early treatment of patients with endometriosis of the large bowel is usually necessary because of obstruction. Management depends on three main factors:

(a) the age of the patient, having in mind the distress caused by castration early in life;

(b) the degree of relief of symptoms, particularly obstruction, which might be expected to follow atrophy of the lesions after castration;

(c) the extent to which endometriosis has involved other pelvic organs.

In a young woman it seems desirable that some ovarian tissue be preserved both to avoid an early artificial menopause and to leave some chance of pregnancy in the future no matter how unlikely it may be. This usually is not possible as in most patients there is extensive endometriosis of the pelvic organs in addition to the lesion obstructing the bowel (Cattell, 1937). Cattell has found that radical treatment is necessary in most patients irrespective of age, that is, removal of the uterus and Fallopian tubes as well as both ovaries. On the other hand he has found resection of the bowel lesion itself rarely necessary. Referring to pelvic endometriosis in general, Dougal (1948) found it possible to conserve some ovarian tissue in only 57 of 262 personal cases. Treatment allowing subsequent pregnancy was possible in only 28 patients of whom 2 eventually did become pregnant.

If the pelvic organs are intact in a young woman resection of the obstructing lesion itself seems to be the logical treatment except for cases in which the only excisional operation would be abdomino-perineal resection of the rectum leaving a permanent colostomy or in cases in which attempts at eradication of the disease might endanger the patient's life

(Macleod, 1946). In women nearing the end of the child bearing years castration is the simplest and safest procedure where the pelvic organs are intact. Castration without resection of bowel resulted in complete restoration of the lumen of the bowel in Jenkinson and Brown's (1943) cases of obstruction due to endometriosis.

Symptoms arising from extensive pelvic endometriosis require treatment in addition to those produced by lesions in the bowel. Most authors agree that it is rarely necessary to resect the obstructed bowel in endometriosis once an artificial menopause has been induced, but in the majority of cases it is not enough just to remove or irradiate the ovaries. Usually removal of the uterus and the Fallopian tubes is also necessary to relieve symptoms arising from them. The menopause, whether natural or artificial, does not finally free the patient of all risks of endometriosis producing intestinal obstruction. Welch (1949) recalled patients in whom endometriosis of the bowel had been asymptomatic until after the menopause. This he believed was due to increasing fibrosis and narrowing of the bowel lumen as the lesions became atrophic after the menopause.

If the diagnosis can be made pre-operatively it is wise to operate only between the menstrual periods at a time when pelvic congestion is likely to be minimal (Masson, 1935).

Both bowel resection and the induction of an artificial menopause were avoided in a case reported by Marshak and Friedman (1950). Their patient, a 34-year-old woman with rectal involvement from a mass in the posterior fornix, was treated by a course of eight weekly injections of testosterone 300 mg. At the end of this course her rectal and pelvic pain had gone, stools which were formerly ribbon shaped returned to normal and the barium enema became normal. There was no virilism. After 3 years the patient had a laparotomy for chronic cholecystitis and a thickening only was palpated at the site of the previous lesion in the bowel. The adnexae were found to be nodular and fixed.

The treatment of this patient was successful, but as a general rule treatment of endometriosis with testosterone is palliative rather than curative and recurrence can be expected.

CASE REPORTS

Case 1

Mrs. S.R., a housewife aged 53 years with one child, presented on 16th December, 1955. On two occasions, seven weeks and three weeks before, she had passed a moderate amount of slimy yellow material tinged with dark stringy blood. She sometimes had a feeling of incomplete defaecation, but at no stage was she constipated. On two occasions approximately one week before presentation she had experienced colicky lower abdominal pain early in the morning. There had been no loss of weight, dysuria nor menstrual abnormality. The menses had occurred regularly every twenty-eight days with a moderate loss over four to five days and accompanied by very little pain.

Examination showed no abnormality. A barium enema demonstrated a constant irregular filling defect in the upper sigmoid region. A provisional diagnosis of carcinoma of the sigmoid colon was made and without further investigation laparotomy was performed on 21st December, 1955. There was a hard rounded tumour 2.5 cm. in diameter incorporated in the wall of the mid-sigmoid and the lumen of the bowel appeared to be obstructed partly by obturation and partly by a constriction of the remaining circumference of the bowel immediately opposite the tumour. The appearance was typical of a constricting carcinoma of the colon. The surface of the mass was puckered and white except for a minute bright red cyst 2 mm. in diameter projecting from the surface. The lymph nodes along the inferior mesenteric artery were enlarged, but there was no other evidence of metastasis. The uterus was normal in size and both ovaries were normal, but the left Fallopian tube was adherent to the pelvic brim on the left side with filmy peritoneal adhesions. The diagnosis of carcinoma of the colon was thus reasonably confirmed and a formal left hemicolectomy performed. The inferior mesenteric artery was divided at its origin. After the operation the specimen was opened and it was found that the mucosa was intact throughout the length of the lesion although it was partially adherent to the outside mass. The cross section of the tumour was creamy yellow in colour with thick strands of dense fibrous tissue running through masses of thickened fat suggesting a chronic inflammation rather than a carcinoma. The patient's convalescence was uneventful. Histological examination proved the lesion to be endometriosis.

Discussion

When the true diagnosis was known the patient was questioned again and it was found that the two episodes of rectal bleeding and discharge had each occurred at the beginning of a menstrual period, two months and one month before operation. This patient's story illustrates the importance of suspecting endometriosis as a cause of obstructive bowel symptoms in all pre-menopausal women. If the history of menstrual periodicity of symptoms had been known prior to operation the appearance of a small red spot on the surface of the lesion might have aroused suspicion and led to an operative biopsy. The surgical treatment may have been changed then from left hemi-colectomy to oophorectomy.

Case 2

Mrs. E.D., a woman of 43 years with no children, was admitted to hospital on 18th February, 1955, in a collapsed state. Six months before she first became increasingly constipated, but after five months she commenced to pass small formed motions at least 3 times in each twenty-four hours. There was no history of rectal bleeding. Two days before admission she developed a dull epigastric pain which later became more severe, colicky, and central in position and it was accompanied by copious diarrhoea and vomiting which continued until admission. Prior to this acute episode there had been no loss of weight, anorexia, indigestion nor dysuria. The menses had recurred every twenty-six days lasting usually five days without pain. The onset of this acute gastro-intestinal disturbance coincided with the onset of a menstrual period.

FIG. IV. Photograph of the operative specimen from Case 2. The lumen of the colon is constricted by endometriosis involving the serous and muscular coats leaving the mucosa intact. Proximal to this lesion the colonic mucosa shows an appearance typical of ulcerative colitis. Distal to the lesion it is normal.

The lips and extremities were blue and cold and the blood pressure was unrecordable, but the pulse could just be felt at the wrist. The abdomen was moderately distended, rigid, and very tender, particularly above and to the left of the umbilicus. The tongue was dry and coated and the breath had a faeculent smell. No further examination was done at this stage and the patient was resuscitated and prepared for laparotomy. The peritoneal cavity contained slightly blood stained fluid and fibrinous flakes covered loops of small bowel and the large bowel which was dilated proximal to a constricting lesion in the upper sigmoid colon. The distal colon was collapsed. This lesion was thought to be a carcinoma and a caecostomy was performed to decompress the obstructed large bowel.

Twelve days later the abdomen was opened again and on this occasion the diagnosis of carcinoma of the colon was clinically confirmed. It was noted that there were no metastases in lymph nodes, peritoneum nor liver. Small diverticula were seen arising from the transverse colon. The inferior mesenteric artery was divided at its origin and a left hemi-colectomy performed. Convalescence was delayed by a wound infection, but the caecostomy was closed on 16th March, 1955, and the patient allowed home on 8th April, 1955.

The specimen was opened longitudinally and it was seen that the mucosa was intact throughout the length of the lesion but the lumen was narrowed over about 6 cm. by a white, gelatinous, extramucosal mass replacing the normal bowel wall. Proximal to this constriction the mucosa was congested, ulcerated, and nodular to the limit of the resection. This appearance was identical with that of non-specific ulcerative colitis (Fig. IV). Histologically the mass showed islands of endometrial glands and stroma embedded in fibromuscular tissue.

Discussion

The exacerbation of ulcerative colitis in this patient coincided with the onset of a menstrual period, but this isolated fact was hardly sufficient to arouse any suspicion that this lesion was not a carcinoma. Perhaps, if operative biopsy had been performed a correct diagnosis may have led to treatment by oophorectomy rather than by the major operation of left hemi-colectomy. It is quite possible that the severity of the ulcerative colitis would have been reduced, if not abolished by oophorectomy, once atrophy of the constricting lesion had occurred and better drainage of the bowel obtained.

Case 3

Miss J.M., aged 29 years, presented on 4th January, 1956, with a history of persistent diarrhoea for ten months accompanied by anorexia and loss of weight. The motions were watery and contained mucus, but never pus nor blood. For one month she had had an aching pain in the anus extending outwards to the left side of the pelvis. There was no history of menstrual irregularity. A hard, immobile mass was felt in the anterior wall of the rectum and it could also be felt high in the posterior fornix of the vagina. The cervix was normal and the uterus was not enlarged. At sigmoidoscopy a red polypoidal mass was seen projecting into the anterior wall of the rectum. The rectal mucosa was not ulcerated (Fig. V). A biopsy showed the presence of endometrium beneath the intact rectal mucosa.

Laparotomy was performed eight days later and a firm irregular mass 7 cm. by 3 cm. was found attached to the anterior wall of the rectum and the posterior vaginal fornix. On the peritoneum of the right lateral pelvic wall were two small black sclerotic areas typical of endometriosis. An anterior resection of the rectum was performed removing in addition a portion of the posterior vaginal wall in front of the tumour. The tissue composing the mass was white in colour and resembled fibrous tissue, but the coats of the bowel could be made out quite clearly. Histological section demonstrated the presence of islets of endometrium throughout the fibrous mass.

FIG. V. Photograph of the opened specimen of rectum from Case 3 showing the polypoidal extra-mucosal mass projecting into the anterior wall of the rectum from the region of the posterior vaginal fornix.

The patient's convalescence was temporarily retarded by the development of a small faecal fistula, but it closed quickly.

Discussion

This was the only patient in the series in whom a pre-operative diagnosis was made. After resection of the lesion had been performed the surgeon wondered whether he should remove the ovaries in this patient particularly as there were other lesions on the lateral pelvic wall, but eventually decided not to. Had this patient been older, oophorectomy would have been all that was necessary to relieve the symptoms. However, she was only 29 years old and so a limited resection of the lesion was preferable to castration. Once the resection had been done there was certainly no indication to remove the ovaries as well in this patient as the pelvic wall lesions were small and were not likely to cause harm for a considerable time.

FIG. VI. Photograph of the operative specimen from Case 4. The upper lesion is a constricting carcinoma and the colon is dilated above it. The distal and lower constriction of the bowel is produced by an eccentric mass of endometriosis leading to obturation and angulation of the lumen of the bowel.

Case 4

Mrs. K.K., a widow of 45 years, was admitted to hospital on 11th September, 1955. For two weeks she had had colicky pain not unlike dysmenorrhoea accompanied by vomiting. Her bowels had not been open since the onset of the pain and for some time just before admission there had been no passage of flatus. Prior to this illness she had been quite well and there was no history of alteration of the bowel habit nor of rectal bleeding. Her menses were irregular in duration and interval and the loss was usually heavy. No mention was made of

dysmenorrhoea. The patient was dehydrated and febrile. The abdomen was distended, tympanitic and generally tender. Rectal examination was normal.

A diagnosis of subacute large bowel obstruction was made and at laparotomy the colon was found grossly dilated up to an annular constriction in the upper sigmoid region. Without further exploration a caecostomy was made through a muscle splitting incision in the right iliac fossa. On 24th September the abdomen was re-opened and 2 annular constricting tumours were found, the first at the lower end of the descending colon and the second in the mid-sigmoid colon. Several small lymph nodes were seen, but none were considered malignant and there was no other evidence of secondary spread from these apparent carcinomata. The inferior mesenteric artery was divided at the aorta and a left hemicolectomy performed.

FIG. VII. Photograph of the external surface of the operative specimen from Case 4. The bowel is seen dilated above the constricting carcinoma. There is nothing characteristic about the appearance of the localized endometriosis in this specimen.

The removed bowel was dilated proximal to the first tumour which was a hard, white, ulcerating mass completely encircling the bowel and constricting it over a distance of 2 cm. This mass extended through to the serosa. Eleven centimetres distal to this tumour was a second mass in the bowel wall 2 cm. in diameter which extended up to, but not through the mucosa. The mucosa was intact throughout the length of this second lesion and the bowel lumen was obstructed only because of the angulation produced by this eccentrically placed mass (Figs. VI and VII). The proximal ulcerating mass was proved to be adenocarcinoma while the distal mass was composed of islets of dilated tubules of columnar epithelium surrounded by a loose cellular stroma embedded in muscle. A diagnosis of localized endometriosis of the colon was made.

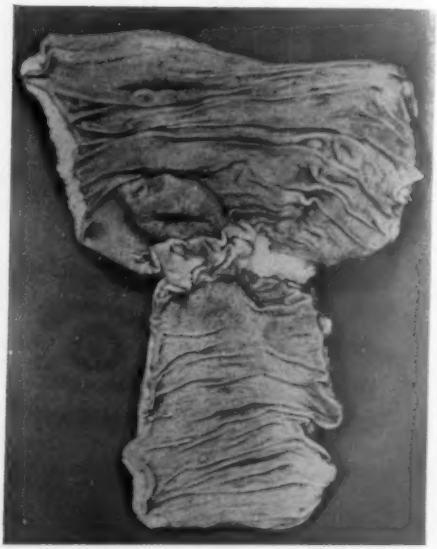

FIG. VIII. Photograph of the operative specimen from Case 5 showing intact mucosa at the site of constriction of the colon except where it has been removed to show the thickening of the remainder of the bowel wall.

Discussion

It was an unfortunate coincidence that this patient should have had both a carcinoma and endometriosis of the colon. In retrospect there was nothing in the history to challenge a confident diagnosis of carcinoma except perhaps the complaint of irregularity of the menses and menorrhagia. Similarly the operative findings raised no doubts and biopsy of each lesion in turn would have been the only way of discovering their differing nature, but of course there was no other possible treatment in this patient as an alternative to that carried out. The operative specimen of this patient provided an interesting comparison of the two diseases to be differentiated.

Case 5

Mrs. J.M.D., aged 37 years, was admitted on 15th August, 1956. She complained that over the previous eleven months she had had attacks of colicky lower abdominal pain, distension and vomiting lasting three to four days. During these attacks

she was constipated, but was aware of intense intestinal activity and passed more flatus than usual. There was no rectal bleeding. These obstructive episodes became much more frequent during the month before admission when the symptoms were almost continuous. Her appetite was normal, there was no weight loss and the menstrual periods were normal. Her appendix had been removed at the age of 10 years and at 27 years the right Fallopian tube had been removed because of a tubal pregnancy. "An abscess of the left tube had been opened" eighteen months before admission.

The abdomen was not distended. A mobile mass was felt in the left iliac fossa which diminished in size on pressure accompanied by a gurgling sound. Rectal examination was normal, but she was found to be tender in the left vaginal fornix in pelvic examination. Sigmoidoscopy revealed nothing abnormal, but a barium enema showed a filling defect in the mid-sigmoid colon which was described as being possibly chronic inflammatory in origin, but neoplasm could not be excluded.

Laparotomy was performed on 16th August. There were dense omental adhesions to the previous abdominal incisions and to the pelvic viscera. There was a hard mass in the mid-sigmoid colon to which the left Fallopian tube was adherent suggesting a carcinoma of the colon with invasion of the tube. The left ovary was not seen. A Mikulicz resection of the sigmoid colon was performed and the resulting colostomy was closed on 5th September. The operative specimen was opened and it was seen that the colon was dilated above and collapsed below a constriction caused by a thickening of the bowel wall. The mucosa of the colon was intact, but the infiltrating white tissue involved the remainder of the wall (Fig. VIII). Histological examination proved the tumour to be endometriosis of the colon.

Discussion

The history and examination as presented did not suggest that this patient had anything other than a carcinoma of the colon. The past history of pelvic disease was not really suspicious and the operative inspection of the pelvic organs raised no doubts. However, further questioning of the patient after the true nature of the lesion was known revealed that she had noticed that the short attacks of subacute bowel obstruction at the beginning of her illness occurred either immediately before or after an otherwise normal menstrual period. In retrospect this knowledge makes important, features which were considered of lesser interest during the first assessment of this patient. The radiologist did not favour the diagnosis of neoplasm; the patient had had a past history of pelvic disease and she was still only 37 years of age. It is possible that this knowledge of menstrual periodicity of symptoms might have led to operative biopsy and perhaps to a correct diagnosis in this patient. Oophorectomy then might have been the treatment of choice rather than resection of the lesion.

CONCLUSIONS

One is not likely to see many cases of endometriosis of the bowel and no doubt errors in diagnosis will continue to be made. In this small series of patients in whom intestinal endometriosis occurred as a localized disease there were only two histories (Cases 1 and 5) which contained the key to correct diagnosis. In both, the patients symptoms had occurred concurrently with the menstrual periods although this was not known until after the operation. In Case 3 the diagnosis was made by pre-operative biopsy, but in Cases 2 and 4 there was nothing to suggest that the obstruction was not neoplastic.

To diagnose endometriosis of the large intestine one must suspect it and make a point of carefully questioning all female patients to discover whether their symptoms have shown some menstrual periodicity even when the diagnosis of carcinoma seems unassailable. In many patients one will be able to make a pre-operative diagnosis particularly in those women with rectovaginal septal lesions and in those in whom the bowel is involved secondarily by extension from adjacent pelvic endometriosis. In most of these cases the symptoms of generalized pelvic endometriosis will give a lead. The diagnosis may be histologically confirmed pre-operatively as in Case 3. If not suspected pre-operatively then it certainly should be suspected after operative exposure of the lesions and confirmed by frozen section examination of biopsy material. Errors in diagnosis are not likely to be made in the group of cases presenting to the gynaecologist, but rather in the cases in which there is a discrete obstructing lesion in the sigmoid colon, independent of pelvic disease. These are the cases which present to the general surgeon.

The chance that the lesion will be endometriosis rather than carcinoma is much greater in women under 30 years of age than in women nearing the end of their childbearing life. Therefore it would appear justifiable to biopsy at operation all apparent carcinomata of the colon in very young women. The possible danger of disseminating a carcinoma by biopsy should make little difference to an already poor prognosis at this age and so should not deter the surgeon from performing a biopsy. Only then will it be possible to avoid radical resections of the large bowel which are increasing in magnitude and are still operations endangering the

patient's life. It is fortunate that endometriosis commences on the serosal surface of the bowel and so one would not consider operative biopsy of a mass which was not involving that surface.

Operative biopsy appears justified in older women only when there is evidence of pelvic endometriosis or when the history and or the appearance of the tumour arouse suspicion. At this age it is most unlikely that the tumour will be an example of endometriosis unless these features are present. The approach to treatment has been summarized in Table 1.

straightforward; (b) by producing a discrete intestinal lesion when it is likely to be mistaken for carcinoma and extensive and unnecessary surgery undertaken to cure it.

3. This problem of diagnosis of the discrete lesion is illustrated by 5 case histories.
4. Endometriosis should be suspected if there is menstrual periodicity of symptoms.
5. It is shown that biopsy at operation of all apparent carcinomata of the colon in young women is justified to avoid errors in diagnosis.

TABLE 1

A PLAN OF THE APPROACH TO TREATMENT OF ENDOMETRIOSIS OF THE LARGE BOWEL

Age	*Pelvic Organs Extensively Involved*	*Pelvic Organs Intact*
Under 35 yr.	Radical removal of the pelvic organs without resection of the bowel.	Resection of the lesion if possible, leaving ovarian tissue intact, if not endangering patient's life.
Over 35 yr.	Radical removal of the pelvic organs without resection of the bowel.	Induction of an artificial menopause by bilateral oophorectomy or irradiation of the ovaries.

In patients in whom a pre-operative diagnosis has been made an artificial menopause can be induced by irradiation of the ovaries to avoid laparotomy. Even so it is probably wiser always to have a look at the lesions of the pelvic organs by laparotomy to confirm the diagnosis of their pathology. Having performed a laparotomy bilateral oophorectomy would then be the logical method of removing ovarian tissue.

SUMMARY

1. The current knowledge of endometriosis of the large bowel is reviewed, emphasizing the features assisting the differential diagnosis between this disease and carcinoma.
2. Attention is drawn to two ways in which endometriosis might involve the bowel: (a) as part of a generalized pelvic endometriosis when the diagnosis is often
6. In most patients it is found that pelvic endometriosis is extensive and requires treatment by hysterectomy and bilateral oophorectomy, irrespective of age. When the pelvic organs are intact it is believed an attempt should be made to conserve ovarian function in a young woman and to treat the lesion by resection. In older women one should avoid a dangerous resection and instead produce atrophy of the lesion by inducing an artificial menopause.

ACKNOWLEDGEMENTS

I wish to thank Mr. W. E. A. Hughes-Jones (Case 1), Mr. Douglas Leslie (Case 2) and Mr. E. S. R. Hughes (Cases 3, 4 and 5) for permission to publish details and photographs of their cases. I am especially grateful to Mr. E. S. R. Hughes for permission to include Figs. V and VI which are to appear in his book "The Surgery of the Anus, Anal

Canal and Rectum" (1956). My thanks are also due to Mr. Robert Zacharin for his advice on certain aspects of this paper.

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STRANGULATED EPIGASTRIC HERNIA

By KENNETH R. COX

Royal Melbourne Hospital

EPIGASTRIC hernia usually consists of a protrusion of extraperitoneal fat through the linea alba in a fairly constant position half-way between the xiphisternum and umbilicus. Less commonly a peritoneal sac also pushes through the defect; associated bouts of pain and occasional intestinal bleeding are referable to complications of the contents.

Strangulation of the contents is rare. Four cases have been recorded in the past thirty years. As with the patient recorded by Brewer and Marcus, bilateral inguinal herniae were present in one case, but they were reducible, and offered no difficulty in deciding the site of intestinal obstruction.

Two personal cases are reported here.

Case 1

W.R., male, aged 57, and occupied as a grocer, was admitted to the Royal Melbourne Hospital on 6th February, 1955, with a painful tender lump in the epigastrium. This lump had been present for nine years and was usually easily reducible. Occasional bouts of tenseness and tenderness had occurred, but never as severe as this attack, which had begun 36 hours previously.

His general condition was good, with a pulse rate of 60 and a pulse pressure of 60. He had not vomited; his bowels had opened that morning 13 hours before admission. Distension or peristaltic waves were not observed. Midway between the umbilicus and xiphisternum was a tense tender lump 8 cm. in diameter, which was irreducible, with no impulse on coughing.

The sac was exposed by a transverse incision over the lump; on opening the sac clear fluid and purple small bowel were seen. The bowel was delivered after a lateral incision into the hernial margin over a director. A small area at the constriction ring was oversewn when bowel viability was established, and the bowel returned to the abdomen. The sac was cleared, ligated and resected. A Mayo type repair was used.

The post-operative course was uneventful apart from inflammation of the conjunctivae for 24 hours.

He was discharged 6 days after operation.

Case 2

D.T., female, a diabetic aged 72, was sent to the Royal Melbourne Hospital on 16th September, 1955, with a diagnosis of strangulated para-umbilical hernia.

The hernia had been present for thirty years and had given no trouble until 24 hours before admission when it swelled to 8 inches diameter. Frequent vomiting began at the same time and some constant pain was felt over the hernia. Five hours before admission the hernia spontaneously diminished in size, and vomiting and pain ceased.

On examination the patient was obese, dehydrated and salt-depleted. There was an irreducible, slightly tender mass over the umbilicus which was not tense and had an impulse on coughing.

Fluids and electrolytes were replaced and the diabetes stabilized. No further vomiting or pain occurred, and the hernia was explored 32 hours after admission.

FIG. I. Photograph of patient (Case 1) before operation.

At operation three separate hernial sacs were found. The largest was a large, irregular epigastric hernia measuring 15 cm. x 10 cm. and placed 8 cm. above the umbilicus. The next was a para-umbilical hernia 6 cm. in diameter, and the last was a small epigastric hernia 5 cm. above and to the right of the umbilicus measuring 2 cm. in diameter. The neck of the large epigastric hernia was cleared and the widened linea alba cut laterally on each side to the rectus muscle. Gangrenous omentum and a gangrenous loop of small bowel were exposed and resected. The defect was closed by a Mayo type

of repair. The other herniae contained omentum only and were rapidly repaired.

Post-operatively she was well for 24 hours, when her temperature rose rapidly, urinary output dropped, respiratory rate rose to 40 per minute; the patient became more drowsy and died 56 hours after operation with a severe bronchopneumonia.

ACKNOWLEDGEMENT

I am grateful to Mr. E. S. R. Hughes for permission to publish these case reports.

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NICHOLAS CULPEPER

HIS TRANSLATIONS OF BARTHOLIN, RIOLAN AND VESLING

By K. F. Russell

Melbourne

ONE of the most prolific writers of books of medical interest in the seventeenth century was Nicholas Culpeper, "Gent. Student in Physick and Astrology." All his books were directed towards a popular rather than a professional audience, but judging by the number of editions that were called for, they were very widely read. Many of his works, indeed almost the majority, were printed after his death, some being re-issued as late as the nineteenth century. He specialized in the translation of various authors from their Latin original into English, thus making available to the public many works which they could otherwise not have read. His notable success in this regard was an English translation of the *Pharmacopœia* issued by the Royal College of Physicians to the intense indignation of the College, for they had the rights to its publication and were loath to see their formulae appear in the vernacular. Many of the earlier editions of his books are of considerable rarity today, for they were so popular they were literally thumbed out of existence. For this reason, too, it is unusual to find any of his works in good condition; this being partly accounted for by the fact that many editions were poorly printed on paper of inferior quality.

Anatomy owes a considerable debt to Culpeper for he was responsible, at least in part, for English translations of the anatomical treatises of Thomas Bartholin (1616-1680), Jean Riolan, the younger (1577-1657) and John Vesling (1598-1649).

Culpeper was born in Kent on 18th October, 1616, "the son of Nicholas Culpeper a Reverend Divine." He was educated in Sussex and later at the University of Cambridge, although, from the account of his life so freely published in his books, it is not clear what subjects he studied while an undergraduate. He came up to London to be "placed with Mr. White, an Apothecary, near Temple Bar," with whom he stayed for eighteen months, later going to a Mr. Drake in Threadneedle Street where, it would appear, he taught his master Latin. He then studied Physick and while it is not clear that he qualified, he certainly became a keen student of Astrology.

About 1640 he set up in practice as a Physician and Astrologer in Red Lion Street, Spitalfields, where, after a successful career, he died on 10th January, 1653/54, aged 38. On his death many unpublished manuscripts of translations were left in the hands of his widow, and, when published, Culpeper's name was associated on the title with that of a co-author. It is not possible to find out how much these posthumous translations owe to Culpeper and how much to his associate. The following epitaph appears in *Culpeper's School of Physick*, 1659:

> Here lies the Doctors' great envy and wonder,
> To the Empericks an aweful clap of Thunder,
> Whom he stript and whipt, for wise men hereafter,
> To make them the scorn and scene of their laughter.
> To their joy sleep here our three Kingdoms sorrow,
> Till the Resurrection bids him, Good morrow.

Of his character the same work says, "Mr. Culpeper was in his Deportment gentle, pleasing and courteous. His complection darkish and swarthy. His Visage rather long than round. Of a Presence not so beautiful as amiable. His Hair black and somewhat curling. His Eyes piercing. His Body a little above a medium, tending to tallness. Of a spare lean Constitution. In his Apparel not exceeding the moderation of one of his degree. Somewhat careless. He was of a clear and establisht Judgement. Of an eloquent and good Utterance. Of a quick spirit, full of swift thoughts and mounting. Of a sparkling ready Wit, a gift which doth not alwayes speak men Fortunate. He was sometimes too much overtaken with deep Speculations, though Melancholly was somewhat contrary to his nature; whatsoever he said otherwise of himself: So that it may rather be imputed to the Crosses of his Life, than to his own

Bartholinus Anatomy;

MADE

From the Precepts of his Father, And from the Observations of all Modern Anatomists together with His own.

With one hundred fifty and three Figures cut in Brass, much larger and better than any have been heretofore Printed in English.

IN

FOUR BOOKS

AND

FOUR MANUALS

Answering to the said BOOKS.

Book I. Of the Lower Belly.
Book II. Of the Middle Venter or Cavity.
Book III. Of the uppermost Cavity, *viz.* The Head.
Book IV. Of the Limbs.

The Four Manuals Answering to the four foregoing Books.

Manual I. Of the *Veins*, Answering to the Fifth Book of the Lower Belly.
Manual II. Of the *Arteries*, Answering to the Second Book of the Middle Cavity or Chest.
Manual III. Of the *Nerves*, Answering to the Third Book of the Head.
Manual IV. Of the *Muscles*, Answering to the Fourth Book of the Limbs.
Also Two Epistles of the Circulation of the Blood.

Published By { *Nich. Culpeper* Gent. And, *Abdiah Cole* Doctor of Physick,

London, Printed by *John Streater* living in *Clerken-well-Close* 1668.

FIG. I. Title page of the 1668 edition of the translation of Bartholin. (Cowlishaw collection.)

A SURE GUIDE;

OR,

The BEST and NEAREST Way

TO

Physick and Chyrurgery:

That is to say,

The *Arts of Healing* by *Medicine*, and MANUAL OPERATION.

Being

An *Anatomical Description* of the whole Body of Man, and its Parts, with their *Respective Diseases*, demonstrated from the *Fabrick* and *Use* of the *said Parts*. In Six Books.

VIZ.

1 *Describing all, and every of the Bones of Mans Body according to the Antient Method.*
2 *Describing the Belly, and all its Parts and Bowels, with their respective Diseases.*
3 *Describing the Chest and all its Parts and Contents, with their respective Diseases.*
4 *Describing the Head, and Face with all their Parts containing and Contained, and their respective Diseases.*
5 *Describing the Limbs of the Body, with the many Ligaments of Muscles, and their Diseases.*
6 *Containing a new Description of the Bones, by a Method first invented by our Author, handling all the Diseases and Symptomes of the said Bones.*

At the End of these Six Books, is added twenty four Tables, Cut in Brass, containing one hundred eighty four Figures, with an Explanation of them; all which are referred to above a thousand places in the Books, for the Help of young Artists.

Written in LATIN, By *Johannes Riolanus*, Junior, Doctor of Physick, Physician in ordinary to the *Queen Mother of France* many years together, and the last she had: And also the *Kings Professor* of *Anatomy* and *Herborisu*, in the University of *Paris*.

The Third Edition, Corrected and Enlarged.

ENGLISHED by *Nicholas Culpeper*, Gent. and *W. R.* Doctor of the *Liberal Arts*, and of *Physick*.

London, Printed by *John Streater*. And are to be sold by *George Sawbridge*, at the Sign of the BIBLE on *Ludgate-Hill*. M. DC. LXXI.

FIG. II. Title page of the so-called third edition (1671) of the translation of Riolan. No copy of a second edition has been traced. (Author's collection.)

disposition. His health was often disturbed with adust Choller. Of Religion he had a greater share than most Physicians use to have; he had so much Zeal as to hate Superstition, and was no friend to Episcopal Innovations. In his Councels he was judicious; of a nimble Apprehension, with little difficulty in his Dispatches. He was a person of so ready a minde, that he could more learnedly and suddenly dictate his Papers for the Press, than some that do take of the Lamp and the Oyl more studiously to contrive them."

Each of the three anatomical texts which Culpeper translated, or helped to translate, was a best-seller of its time, all being most popular with students and graduates alike and all going through many editions in their original Latin.

The first to be translated and published was John Vesling's *Syntagma Anatomicum*, the original edition of which was published in Frankfurt in 1641, the first illustrated issue being published by Frambotti in Padua in 1647. It is probable that Culpeper used the latter edition for his translation which appeared with the title:

> The Anatomy of the Body of Man; Wherein is exactly described every Part thereof, in the same manner as is commonly shewed in Publick anatomies. And for the further help of young Physitians and Chyrurgions, there is added very many Copper Cuts, far larger than is printed in any Book written in the English Tongue. Also Explanations of every particular expressed in the Copper Plates. Published in Latin by Joh. Veslingus, Reader of the Publick Anatomy in the most Famous University of Padua; And Englished By Nich. Culpeper, Gent. Student in Physick and Astrology, living in Spittle-fields neer London.
>
> LONDON: Printed by Peter Cole in Leaden-Hall, and are to be sold at his shop, at the sign of the Printing-Press in Cornhil neer the Royal Exchange, 1653.
>
> *Collation.* Portrait : Title : 6 leaves : pp. 1-92 [pp. 79-92 are numbered 179-192] : 24 leaves : : 24 plates. Quarto.
>
> Another edition:
>
> LONDON: Printed for George Sawbridge, at the Bible on Ludgate-Hill, M.DC.LXXVII.
>
> *Collation.* Title : 3 leaves : pp. 1-92 [pp. 79-92 numbered 179-192] : 24 leaves : : 24 plates. Quarto.

This is the only occasion on which Vesling's work has been translated, the plates being very faithful copies of the originals and, as we shall see later, Culpeper used these plates again in his translation of Riolan's book.

The next to appear was his translation of Jean Riolan's *Encheiridium Anatomicum et Pathologicum* possibly from the Leyden edition published by Wyngaerden in 1619; the full wording of the title being shown in Fig. I.

> A sure guide; or the best and nearest way to Physick and Chyrurgery; That is to say, the arts of healing by medicine and manual operation. Being an anatomical description of the whole body of Man, and its parts with their respective diseases, demonstrated from the fabrick and use of the said parts. In six books . . . Written in Latine, by Johannes Riolanus, Junior . . . Englished by Nich. Culpeper, Gent. and W. R. Doctor of the Liberal Arts, and of Physick.
>
> LONDON: Printed by Peter Cole, and are to be sold at his shop at the sign of the Printing-Press in Cornhil, neer the Royal Exchange, 1657.
>
> *Collation.* Title : 5 leaves : pp. 1-288 : 6 leaves : 24 leaves : : 24 plates. Quarto.
> [pp. 143-190 are dropped in pagination.]
> The plates are identical with those in the translation of Vesling, 1653, and with those in Vesling's original *Syntagma*, 1647.
>
> Another edition:
>
> LONDON: Printed by John Streater, And are to be sold by George Sawbridge, at the sign of the Bible on Ludgate-Hill. M.DC.LXXI.
>
> *Collation.* Title : 3 leaves : pp. 1-288 : 6 leaves : 24 leaves : : 24 plates. Quarto
>
> [pp. 143-190 are dropped in pagination and pp. 33, 40, 119, 122, 123, 126, 127 and 209 are wrongly numbered.]
>
> This is called the third edition, but no trace has been found of a second issue.

When this translation came out Culpeper was, of course, dead and the identity of W.R., his co-author, is uncertain. The British Museum Catalogue suggests he was W. Rand, but it is not unlikely that it was W. Rowland who helped Culpeper with the translation of Riverius' *Practice of Physick*. The translation of Riolan is a good one and in the address to the Reader, Culpeper says:

> A Physitian will not quarrel with his Patient, because he refuseth to take the Pill unless Gilded, nor will we quarrel with any Reader whose want of judgment or misapprehension misguides him to the finding of faults only, but pitty him that his narrow capacities should so impotently desire that all others should be constituted after his size. And this is an ungrateful

folly when men are unwilling that others should endeavour to further their good, because they could not prescribe the method for doing it; these should consider, that there are some in the world whose understanding outstrips theirs, and delight in such things as they contemn; if, therefore, you be pleased with what I have done, I shall not be discontented; but if you be profited too, then I shall believe that I have not labored in vain.

Farewell.

The last of the three anatomical translations was published in 1663. This was an English version of Thomas Bartholin's *Anatomia ex Caspari Bartholini parentis institutionibus* which had appeared in a number of editions with variant titles from 1641. Culpeper's translation had the following title (see Fig. II).

> Bartholinus Anatomy; made from the precepts of his Father, and from the observations of all modern anatomists; together with his own, with one hundred fifty and three figures; cut in brass, much larger and better than any have been heretofore printed in English . . . Published by Nich. Culpeper, Gent. and Abdiah Cole, Doctor of Physick.
>
> LONDON: Printed by Peter Cole Printer and Bookseller at the sign of the Printing-Press Cornhil neer the Royal Exchange. 1663.
>
> *Collation.* Title : 6 leaves : pp. 1-377 : 1 leaf : : 73 illustrations, including 4 folding plates. Quarto.
>
> [pp. 171-300, 329-332 are dropped in pagination.]
>
> Another edition:
>
> LONDON: Printed by John Streater living in Clerken-well-Close, 1668.
>
> *Collation.* 1 leaf (Books newly Imprinted) : Title : 2 leaves : pp. 1-377 : 1 leaf : : 73 illustrations, including 4 folding plates.
> [pp. 171-300, 329-332 are dropped in pagination and pp. 83, 321, 360 are wrongly numbered.]

How much of this work, and indeed the Riolan, was translated by Culpeper himself cannot be estimated for both were printed after his death. Abdiah Cole (1610?-1670?) who was associated with Culpeper in the Bartholin venture also helped him in other translations. He calls himself "Doctor of Physick," but if, or where, he graduated is not known. He may have been a relative of the Peter Cole "Printer and Bookseller at the sign of the Printing-Press in Cornhil neer the Royal Exchange" who printed so many of Culpeper's books. Criticism of Culpeper's translations would be unworthy for they are the only appearances in English of three of the most popular text books of their time, and he deserves everlasting credit for this fact alone. The plates used in his translation of Bartholin are excellent copies of the originals which, themselves, were borrowed, mainly without acknowledgement, from Vesalius, Casserius, Vesling, Folius, Bauhin, and others.

Bibliographically, all of Culpeper's works are notoriously difficult to collate for there is ample evidence of careless, even hurried, typesetting and shoddy printing. They were so popular that it would almost appear the printers were unable to keep up with the demand and most of the so-called editions were really re-issues without any attempt at the correction of obvious typographical faults.

As an indication of the extent of Culpeper's authorship there are no less than 98 entries under his name in the British Museum Catalogue, these including not only the various editions of his many works, but also cross-references to others in which he is mentioned.

ACKNOWLEDGEMENT

Thanks are due to Miss Madeline Stanton of the Yale Historical Medical Library for supplying details of the Yale copy of the 1663 Bartholin. This is one of the very few copies of this edition in existence.

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Books Reviewed

OUTLINE OF ORTHOPAEDICS.

By JOHN CRAWFORD ADAMS, M.B.(Lond.), F.R.C.S. (Eng.). First Edition. Edinburgh: E. & S. Livingstone Ltd., 1956. 8½" x 5½", 423 pp., 299 illustrations. 32s. 6d. net.

In his preface, the author points out that his book is intended primarily to help students who are preparing for qualifying examinations.

With this in view, the presentation is highly systematic, clear and concise, and well adapted to its purpose. The first chapter, on clinical methods, contains a short but useful scheme of examination, and this approach is repeated in the later chapters which are devoted to regional orthopaedics. This is a valuable feature of the book. The second chapter is a condensed general survey of orthopaedic disorders, occupying about one hundred pages. The rest of the book considers these disorders in the regions in which they occur, and in rather more detail.

It is a difficult task to write an orthopaedic text book for students. One can write too much or too little very easily. The book under review is one in which pruning of unwanted knowledge has been carried out vigorously. This has produced a volume of handy size, and smaller than many similar text books, which is a real advanage. Many may feel, however, that this condensation has gone too far, leaving at times a rather bald and uninteresting description. For example, the cause of congenital torticollis is dismissed in three lines, while the consideration of such matters as scoliosis, poliomyelitis or congenital dislocation of the hip is reduced to an outline. Perhaps this must be the price paid if a speciality such as orthopaedics is to presented within the capacity of an undergraduate.

PULMONARY CIRCULATION AND RESPIRATORY FUNCTION. — A Symposium.

By Sundry Contributors. 1st Edition. Dundee: D. C. Thomson & Co. Ltd., Dundee, 1956. Distributed by E. & S. Livingstone Ltd., Edinburgh and London. 10" x 7¼", x plus 44 pp., 12 diagrams, 1 plate Price: 12s. 6d. stg.

This book comprises the papers and discussion at a symposium held in September, 1955, at the University of St. Andrews. A large group of those in Britain interested specially in the lungs, physiologists, pathologists, physicians and surgeons, took part, including Dr. Averill Liebow, Professor of Pathology at Yale University, who was the Praelector in Pathology at the University of St. Andrews for 1955.

The result is a fascinating collection of the latest ideas on lung circulation and function. The state of knowledge of these complex subjects being what it is, it is natural that the papers should present more problems than they solve, but they are none the less stimulating. The dry humour of the practical physician, Dr. Robert Coope, with his gentle ridicule of the tendency of the more scientific to favour mathematical complexities gave just the right balance to the symposium. Those of us who wish we might have been there may share the experience by reading this book.

SIR JOHN BLAND-SUTTON, 1855-1936.

By W. R. BETT, M.R.C.S., L.R.C.P. Edinburgh: E. and S. Livingstone Ltd., 1956. 8½" x 6½", viii plus 100 pp., portrait and 5 plates. Price: 20s. stg.

On the 22nd April, 1955, the Middlesex Hospital celebrated the centenary of the birth of John Bland-Sutton when notable addresses were given by Sir Gordon Gordon-Taylor and Lord Webb-Johnson and an excellent exhibition was arranged to honour its famous surgeon and benefactor. Gordon-Taylor's eulogy on that occasion will long be remembered and now Mr. W. R. Bett has written a biography of the man who, from very humble beginnings, carved out for himself so adequate a niche in the history of modern surgery. It is fitting that this should appear now to round off the Middlesex celebrations.

Mr. Bett gives us a short but well-written account of his life and labours and presents the many facets of his career as anatomist, both human and comparative, as surgeon and as benefactor. Bland-Sutton endeared himself to his many friends and students in spite of (or was it because of?) his unusual character and forcefulness and it is obvious from this book that the author was one who came under the spell of this remarkable man. Many of Bland-Sutton's writings can be re-read with pleasure today, for he was a stimulating writer who pressed home his point with dogmatism and a fund of anecdote; his lectures must have been a delight. He had the rather charming habit of expressing himself in doggerel; the best known example of which was written on the occasion of his last operating day at the Middlesex. The theatre was crowded and after the last case he walked over to the wall and wrote on the slate:

"I feel too sad to talk,
So write my thoughts in chalk
Upon the wall.
Nurses well-trained and kind,
Better no man could find.
Farewell all."

His monument is the Middlesex which he served for so long, and where his ashes now rest; his influence can still be seen in the Royal College of Surgeons for much of the furniture of that noble edifice came from his house and they received the bulk of his estate on the death of his wife.

This tribute to the memory of Bland-Sutton can be thoroughly recommended to every surgeon and the author deserves the thanks of us all for the time and energy that have gone into its production.

Books Received

THE CHRISTCHURCH HOSPITAL MEDICAL MANUAL.

By Sundry Authors. Edited by C. T. HAND NEWTON, M.D., F.R.A.C.P. F.R.C.S.(Edin.). 4th Edition. Christchurch, New Zealand: N. M. Peryer Limited, 1956. 7¾" x 5", 175 pp., 10 tables. Price: 21s. net.

THE FACTS OF MENTAL HEALTH AND ILLNESS.

By K. R. STALLWORTHY, M.D., Ch.B. First Edition. Christchurch, N.Z.: N. M. Peryer Limited, 1956. 5½" x 8½", 215 pp. Price: 18s. 6d.